









# SAJOUS'S ANALYTIC CYCLOPEDIA OF PRACTICAL MEDICINE

BY  
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# SAJOUS'S

## ANALYTIC CYCLOPEDIA

### of PRACTICAL MEDICINE

**CANNABIS INDICA** (Indian Hemp; Hashish).—This consists of the dried flowering tops of the pistillate or female plants of *Cannabis sativa*, an herb of the family Moraceæ, growing in India, Persia, southern Europe, America, and Africa. For a long time the strongly active hemp of India was believed a species distinct from the common hemp, and the name *Cannabis indica*, therefore, applied to it. It is now known, however, to be the identical plant, differing from ordinary hemp merely in the greater amount of pharmacologically active principle contained in it. The plant, indeed, attains its highest therapeutic power when grown in tropical or subtropical climates, inasmuch as it develops there a larger content of resin than elsewhere. Hemp imported from India is, however, by no means essential for good therapeutic results, Houghton and Hamilton having found (1908) samples grown in various localities of the United States and Mexico to be fully as active, clinically and experimentally, as the best imported hemp.

In the Orient the *churrus*, *charas*, or resinous exudation of cannabis is smoked and also introduced into an

intoxicating drink. The Arabian *hasheesh* and Hindoo *bhanga* are practically identical, being aromatic confections of which hemp forms the essential part. Another common way in which the drug is taken is in a sweetmeat of a green color, made with flour and various other ingredients.

The active constituent of cannabis is a reddish-brown oil or resin, generally termed *cannabinol*. According to Fränkel, the active substance is a phenolaldehyde the chemical formula of which may be expressed thus:  $\text{OH.C}_{20}\text{H}_{28}\text{COH}$ ; cannabinol, however, appears to be merely a mixture of several resins and volatile oils, the exact nature of most of which has not as yet been determined. Wood, Spivey, and Easterfield described the entire resinoid exudation of Indian hemp as consisting of a terpene, a sesquiterpene, a paraffin, and cannabinol itself, of which they obtained 33 per cent. from one specimen of the "charas" and 16 per cent. from another. In common with other resins, cannabinol is insoluble in water, but dissolves in alcohol, ether, chloroform, and oils. Choline is also known to be a constituent of cannabis; likewise is, possibly, the crystal-



line substance *cannabinc*, which is considered to be an alkaloid. Other alleged components of cannabis probably represent simply modifications of the mixture "cannabinol" arising through different methods of isolation. The whole subject of the chemical constitution of cannabis is still in a state of uncertainty and confusion. According to Lees, watery extracts of the drug contain some active ingredient.

### PREPARATIONS AND DOSE.—

Following are the official preparations of cannabis, in addition to the crude drug, *Cannabis*, U. S. P., the dose of which is 1 grain (0.06 Gm.) :—

*Extractum cannabis* (extract of cannabis). Dose,  $\frac{1}{6}$  to 1 grain (0.01 to 0.06 Gm.).

*Fluidextractum cannabis* (fluidextract of cannabis). Dose,  $1\frac{1}{2}$  to 5 minims (0.09 to 0.3 c.c.).

*Tinctura cannabis* (tincture of cannabis), 10 per cent. Dose, 12 to 30 minims (0.8 to 2 c.c.).

The first-named quantity under each of these preparations is the official dose. Since hemp preparations are very subject to deterioration, however, the larger dose mentioned will not infrequently have to be attained before the desired therapeutic effects appear.

Some of the unofficial preparations containing or derived from cannabis indica are as follows:—

*Mistura chloroformi et cannabis composita*, N. F. IV ("chloroform anodyne"), 1 fluidram (4 c.c.) of which contains approximately  $7\frac{1}{2}$  minims (0.5 c.c.) of chloroform, 11 minims (0.75 c.c.) of tincture of cannabis indica,  $\frac{1}{4}$  grain (0.009 Gm.) of morphine sulphate, and 2 minims

(0.12 c.c.) of tincture of capsicum. Dose,  $\frac{1}{2}$  fluidram (2 c.c.).

*Mistura chlorali et potassii bromidi composita* (chloral and bromide compound), 1 fluidram (4 c.c.) of which contains about 12 grains (0.8 Gm.) each of hydrated chloral and potassium bromide, and  $\frac{1}{8}$  grain (0.008 Gm.) each of the extracts of cannabis indica and hyoscyamus. Dose, 1 fluidram (4 c.c.).

*Pilula antineuralgica* (Brown-Séquard), containing the extracts of hyoscyamus, conium, ignatia, opium, aconite, stramonium, and belladonna, with  $\frac{1}{4}$  grain (0.016 Gm.) of extract of cannabis indica. Dose, 1 pill.

*Collodium salicyli compositum*, N. F., (corn collodion), consisting of salicylic acid, 11 parts, and fluidextract of cannabis, 10 parts, in flexible collodion, enough to make 100 parts. Used locally.

Cannabine, a dark-brown, viscid mass, with the odor of hemp, soluble in alcohol and ether; believed to be an alkaloid. Dose, 1 to 4 grains (0.06 to 0.25 Gm.).

Cannabine tannate, a yellowish-brown powder, having a strongly astringent, somewhat bitter taste. It is very slightly soluble in pure water or alcohol, but dissolves more readily in these fluids when an alkali has been added to them. Dose, 4 to 15 grains (0.25 to 1 Gm.).

Cannabinon, a preparation of the resinous mixture cannabinol, having a disagreeable taste. Dose,  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 Gm.).

Cannabindon, a dark, cherry-red syrup, with an unpleasant taste and insoluble in water. Dose,  $\frac{1}{2}$  to 1 minim (0.03 to 0.06 c.c.).

Cannabinine, a brownish, syrupy liquid with an odor similar to that of

nicotine. Dose,  $\frac{1}{4}$  to 1 minim (0.015 to 0.06 c.c.).

These preparations, though claimed to be superior to the official ones in that a closer approximation is made to the true active constituent of the drug, appear to deteriorate with the same readiness, and do not offer any marked advantage over the galenical drugs. Chemical methods of assaying cannabis products not being practicable because of the prevailing uncertainty concerning the nature and number of the contained active substances, a biological procedure for standardization, consisting in the injection of the drug in dogs and observation of the amount of drug required to cause a given degree of inco-ordination, has been generally adopted, which gives reliable, though only approximate results. The physician prescribing cannabis should by preference use recently standardized products, as preparations kept for any length of time are likely to have undergone considerable deterioration. It is said that, in India, dealers in the drug refuse to buy the old crops of cannabis after the new ones are gathered, and that after two years the crops are publicly burned. Biological standardization in dogs of the U. S. P. cannabis preparations is now (1919) officially required.

American hemp contains the active constituent. If equal care is exercised in selecting the proper part of the drug for extraction, no material difference in activity will be found between extracts of Indian and American hemp. It may be used instead of the imported article. Hamilton (Jour. Amer. Pharm. Assoc., Apr., 1915).

**MODES OF ADMINISTRATION.**—The preparations of hemp are active only when given by mouth

or rectum. When administered subcutaneously the resin remains unabsorbed, no effect being, therefore, produced. The fluidextract or tincture of the drug may be given either in an alcoholic flavored preparation (with a little chloroform—Goodwin), on a piece of moist sugar (washed down with water), or in a small quantity of wine. The extract is employed where the remedy is to be given in pill form. Where no standardized preparation is available, the initial dose should be small, as some specimens prove unexpectedly powerful.

Goodwin advises that, as a rule, cannabis indica be not given to a patient unless the latter has confidence in the physician, and that in giving any but the smallest doses the patient should be forewarned that some peculiar symptoms might arise, though also assured that there would not be the slightest danger.

**INCOMPATIBILITIES.**—Addition of even small amounts of water to alcoholic preparations precipitates the active resin cannabinol. Acids, strong alkalies, and strychnine are also incompatible.

#### **PHYSIOLOGICAL ACTION.**

**Nervous System.**—The action of hemp on the brain consists of a combination of depression with stimulation, the latter being most marked in the initial stage of the effects and when large doses are used. Like opium, cannabis tends to plunge the patient into a condition of semiconsciousness, with loss of the power of judgment, but great activity of the imagination. Continuity of thought becomes impossible, and the subject, impelled at first to unusual physical activity, associated with a feeling of unwonted well-being, may execute

various senseless acts, talk at random, and exhibit merriment to an absurd degree. Especially characteristic is a loss of the power of appreciating distance and time, near objects generally seeming remote and minutes lengthened to hours. With small doses, these evidences of primary stimulation are frequently absent or but slightly marked—especially in European races, in contradistinction to Orientals—and the drug acts chiefly as a hypnotic and analgesic. After a period of drowsiness the patient passes into a quiet sleep, from which he finally awakes, after a variable interval, without experiencing any unpleasant after-sensations of languor, nausea, or headache.

In addition to its effects on the intellectual functions, cannabis indica exerts a distinct action of peripheral sensation. The pain sense is obtunded or abolished and the tactile sense rendered less acute. More or less pronounced numbness and tingling may precede these effects. That the motor portions of the nervous system may also be influenced is shown by the increased movement and even convulsions sometimes observed after large doses, as well as the inco-ordination seen in dogs to which the drug has been administered for purposes of standardization. In frogs, sensation is lost before the power of voluntary movement.

According to Dixon, the effects of hemp vary with the mode of its introduction into the system. Exhilaration is most manifest when the drug is smoked; where it is taken by the mouth in small amounts exhilaration does not generally occur. Dixon states that inhalation of the drug will remove the sensations of muscular

fatigue which follow hard physical labor, and act as a cerebral stimulant.

**Circulation.**—Ordinary doses of cannabis indica, taken internally, produce little, if any, change in the circulatory functions, though inhalation of the drug is capable of accelerating the heart action. Large doses tend likewise to increase the cardiac rate, probably in part owing to the increased motor activity induced. Poisonous amounts have been shown by Dixon to cause death by circulatory rather than respiratory failure.

**Alimentary Tract.**—Unlike most opiates, cannabis does not disturb digestion and bring on constipation. It appears often to increase the appetite; the reason for this is not as yet definitely known.

**Kidneys.**—Cannabis has been credited with possessing a diuretic effect, though this is probably never very marked. According to Dixon, fresh hemp is diuretic, while the dried plant exerts but little such action.

**Other Effects.**—The drug tends to dilate the pupils. It sometimes acts as an aphrodisiac, and has been stated to stimulate the uterine contractions where there is inertia. Locally, it is believed to possess slight analgesic properties.

**ABSORPTION AND ELIMINATION.**—Cannabis indica is absorbed slowly from the gastrointestinal tract, one or two hours elapsing before its effects appear. It is not absorbed when given subcutaneously. Elimination of the drug is likewise slow; after full doses the effects may persist twenty-four or thirty-six hours. The chief channel of elimination appears to be the urinary tract.

**POISONING BY CANNABIS INDICA.**—Large single doses of

Indian hemp induce to an exaggerated degree the mental disturbances already noted under Physiological Action. Marked exhilaration, inordinate laughter or singing, great restlessness, and accelerated heart action are characteristic of the earlier stage of its action. These are followed by numbness of the limbs, anesthesia of the skin, inco-ordination, not infrequently a fear of impending death, sometimes more or less marked convulsive phenomena, and then profound sleep or coma. Bicknell reported a case in which there was a sensation as of extreme tension in the abdominal blood-vessels, which felt distended almost to bursting. After extremely large doses depression of the circulation and respiration may appear, but death from cannabis indica poisoning is, to say the least, very rare, no case terminating fatally from this cause having apparently been recorded. Houghton and Hamilton injected 2 ounces of the U. S. P. fluidextract into the jugular vein of a dog; after being unconscious about a day and a half, the animal recovered completely.

Cases reported of 2 brothers, aged 20 and 22, each of whom took 90 minims (5.55 c.c.) of tincture of cannabis indica. Different effects were produced in the two cases: In the younger, the beginning of the period of excitement was delayed for some little time and its onset was gradual. The effect of the drug wore off slowly, the pupils remaining dilated for four days. There was a fresh outburst of excitement twenty-four hours after the taking of the drug, following an apparently normal period of ten hours. In the elder brother the onset was almost instantaneous, excitement reaching a climax at once. Later this gave way to extreme mental depression and numbing of sensa-

tion. In only 1 case was sleep accompanied by dreams. In neither case did the drug produce its reputed aphrodisiac action. James Foulis (Edinburgh Med. Jour., Sept., 1900).

**Treatment of Poisoning.**—Tannic acid and an emetic may be given to remove from the body whatever portion of the poison is still unabsorbed. The administration of lemon juice has been recommended. If circulatory or respiratory depression should happen to appear, stimulants such as caffeine, digitalis, and strychnine may be given, external heat applied, and artificial respiration practised if necessary.

**Chronic Poisoning, or "Hashish Habit."**—This is observed almost exclusively in eastern countries, where hashish is employed in the form of a beverage for purposes of intoxication. Persistent overuse produces a condition of general functional incapacity characterized by reduction or loss of the will power and ability to concentrate the attention, stupor and physical weakness, tremor, anorexia, pallor, yellowness of the eyeballs, diminished peripheral sensation, and loss of sexual power. If the abuse be further continued, insanity, in the form of chronic mania or melancholia, supervenes. In some cases a form of delirium analogous to delirium tremens, and accompanied by terrifying hallucinations and a tendency to destructiveness, is seen. The nutrition of the body appears to be, in general, less seriously affected by chronic hashish abuse than in opiumism, possibly because there is less interference with the digestive functions.

The moderate use of hemp drugs is practically attended by no evil physical effects. Excessive use, however,

does cause injury, tending to weaken the constitution and render the consumer more susceptible to disease, possibly dysentery and bronchitis. Moderate use produces no injurious effects on the mind, except in cases of marked neurotic diathesis. Excessive use both indicates and intensifies mental instability. It tends to weaken the mind, and may even lead to insanity, especially in cases where there is already weakness or hereditary predisposition. Report of Indian Hemp Drugs Commission (Therap. Gaz., April, 1905).

There is no proof that cannabis-indica extract by itself, taken internally or even smoked, causes a habit, and to continue to list it with such habit-forming drugs as morphine, chloral, and alcohol greatly detracts from whatever value it might possess as a sedative. M. V. Ball (Therap. Gaz., Nov., 1910).

**THERAPEUTICS.—As a Sedative or Hypnotic.**—In **insomnia** due to nervous exhaustion, Indian hemp is a useful, though somewhat uncertain, remedy. In **senile insomnia**, with a tendency to wandering and temporary mental aberration, the use of the drug in moderate doses has been highly lauded by Reynolds; likewise, in the occasional nocturnal restlessness of paretics. While its effect cannot be relied upon to the same extent as that of opium, it possesses over the latter drug the advantages of not disturbing the gastrointestinal functions and of not causing headache, nausea, or lassitude, and may therefore in a certain proportion of cases prove preferable to it.

One of the chief uses of cannabis indica for somnifacient purposes is in certain forms of insanity, viz., **melancholia** and **mania**. In the former it has, in addition, been credited with the power of converting mental de-

pression into exaltation. In **delirium tremens** the drug has also been used with some degree of success. It tends to dissipate the horrors and overcome the nervous hyperesthesia. In **chorea** the use of cannabis has been recommended by Suckling. In **tetanus** and **rabies** good results have also been reported.

Cannabis indica used in **delirium tremens** for forty years without the loss of a single case. In alcoholic mania the drug also proved satisfactory. E. B. Silvers (Med. Bull., April, 1907).

In the form of vasomotor coryza popularly denominated "**hay fever**" or "**hay asthma**," the employment of cannabis indica has been suggested, for the purpose of allaying the excessive irritability of the nervous system.

In **bronchitis**, **pulmonary tuberculosis**, and other forms of respiratory disease associated with throat irritation and cough, cannabis indica may be used with advantage as one of the ingredients of a cough mixture. According to Lees, it occupied a place in this connection which cannot be filled by any other drug, as it tends both to alleviate the paroxysms of coughing and exert a stimulating effect. It relieves tickling sensations in the throat and is superior to opium in that no digestive disturbance or other unpleasant side-effect is produced.

Other affections in which the sedative properties of this drug have been utilized include **paralysis agitans**, **exophthalmic goiter**, **spasm of the bladder**, whether of nervous or inflammatory origin, and **gonorrhea**, in which the symptom **chordee** may be relieved by it. It is also said to reduce the amount of pus formed in the last-named disease.

**As an Analgesic.**—*Cannabis indica* has come into widespread use as a remedy for pain of various kinds, more especially in the **headaches** attending migraine, eye-strain, the menopause, and even brain tumors or uremia. In true **migraine** it was formerly used extensively in combination with gelsemium for the purpose of arresting the attacks. It may also be used alone in a full dose to abort a paroxysm, or in small doses three times daily for some weeks to prolong the intervals between attacks (Goodwin). In "sick headaches" Murrell advises that the extract of cannabis be administered in doses of from  $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 Gm.) in pill form. When the patient is suffering constantly from headache, or is liable to an attack on the slightest provocation, such a pill may be taken three times a day for weeks at a time without fear of the production of any untoward effect.

It is especially in pain due to direct involvement of the nerves, rather than in pain associated with inflammatory conditions in general, that cannabis is effective as an analgesic. In **tic douloureux** and other **neuralgias**, the drug has often been found efficient. In **gastric ulcer** Suckling has seen it increase the efficacy of silver nitrate when given in combination with it. In **gastralgia** a pill combining cannabis with bismuth may be used.

Reynolds employed the drug with success in the lightning pains of **tabes**, and it has also been recommended in **multiple neuritis**. In certain malarial states associated with severe headache and nervous symptoms, cannabis is said to be a useful adjuvant to quinine.

*Cannabis indica* is an invaluable remedy in the treatment of disturbances of the sensory centers. It is one of the best remedies in **headaches** of many kinds, and is especially useful in cephalic sensations so common in individuals of neurotic habit. Tincture or fluidextract preferred; 5 to 10 drops (0.3 to 0.6 minim) of fluidextract may be taken on moist sugar, swallowed with a draught of water. Angel Money (Austral. Med. Gaz., Feb., 1900).

With a few exceptions, the efficacy of cannabis indica is limited to those diseases directly traceable to nervous derangement. **Pain** not due to distinct pathological lesions forms the chief indication for its administration, and relief is usually obtained promptly. H. W. Lewis (Merck's Archives, July, 1900).

In various uterine disturbances associated with pain, as **nervous** and **spasmodic dysmenorrhea**, **subinvolution**, and chronic inflammatory states, cannabis indica appears to exert a distinctly useful effect. Not only is pain relieved, but hemorrhage, where present, diminished or arrested. Therefore in **menorrhagia** and impending **abortion** the drug may also prove useful. It is said to be efficacious as a preventive of **post-partum hemorrhage**, but requires to be given in full doses and, with advantage, in conjunction with ergot. For chronic ovarian hypersensitiveness, cannabis indica may also be used with benefit.

Following suppository recommended for **dysmenorrhea**:—

**R** *Ext. cannabis indica*,  
*Ext. belladonna foliorum* .....ãã gr.  $\frac{1}{4}$  (0.015 Gm.).  
*Olei theobromatis* ..... q. s.  
 Ft. suppos. no. j. Da tales no. xx.

**Sig.:** Introduce one every evening, commencing with the fifth day before the menses. V. Robinson (from Jour. de méd. de Paris; Med. Rev. of Rev., March, 1912).

In **acute articular rheumatism** the analgesic property of cannabis has also occasionally been utilized.

In skin affections associated with intense itching, such as **eczema** and **senile pruritus**, the internal administration of Indian hemp will often give relief where local applications fail. It is best, perhaps, to give it in small doses at first and gradually increase (Mackenzie). According to Reynolds, the drug will relieve tingling, formication, and numbness in **gouty** subjects.

According to Aaronsin, cannabis indica may be employed locally with good effect for the relief of **dental pain**. The tincture is diluted with 3 to 5 parts of alcohol and introduced into the cavity of the tooth by means of a tampon of cotton. Such a tampon may also be placed about the gums below the tooth. If the alcohol proves irritating the preparation should be diluted with hot water. It must be stated that Aaronsin's recommendation constitutes only an isolated observation in favor of the use of cannabis as a local anesthetic, which appears to be discountenanced by other authors owing to a supposed primary irritating action of the drug which precedes the local anesthetic effect.

**Other Uses.**—In certain disorders the use of this drug was recommended by Germain Sée. Thus, in **gastric neuroses** and **dyspepsia**, respectively, it tends to allay pain and improve the appetite. In the presence of **hyperchlorhydria**, according to the author

mentioned, it acts as a **sedative** and improves digestion. Alkalies and purgatives should be used in conjunction with it. In the pronounced **anorexia** following exhausting diseases, from 5 to 10 minims of the tincture of cannabis indica, or  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.015 to 0.03 Gm.) of the solid extract given three times daily before meals, will often cause a return of the appetite in two or three days (McConnell). The drug is superior to opium for use in most gastric disturbances in that it does not tend to constipate.

For **pulmonary tuberculosis**, when accompanied by insomnia and dyspepsia:—

**R Strychnine**

*sulphatis* ... gr.  $\frac{2}{3}$  (0.043 Gm.).

*Ext. opii* .... gr. j (0.065 Gm.).

*Ext. cannabis*

*indica* ..... gr. iss (0.1 Gm.).

*Phenylis sa-*

*licylatis* .... gr. c (6.5 Gm.).

*Aloini* ..... gr. ss (0.032 Gm.).

M. et pone in capsulæ no. xx.

S. G. Bonney (Med. Rev. of Rev., March, 1912).

In **intestinal indigestion**, with diarrhea, and in dysentery, the drug may also be of great service, tending to diminish local irritability and excessive peristalsis. In the Orient, cannabis has long been a favorite remedy for **Asiatic cholera**. Here it appears to act, however, rather through temporary stimulation of the nerve centers, tending to revive the patients from collapse, than upon the intestinal condition. According to Marshall, the beneficial influence of cannabis in **menorrhagia** and **dysentery** is due not to the active substance, cannabinol, but to the terpenes it also contains.

In **nephritis, acute or chronic**, can-

*nabis indica* has been stated to overcome **hematuria** and pain, when these symptoms are present.

In **diabetes mellitus** *cannabis indica*, used continuously, will often cause a marked improvement in all the symptoms, without checking the secretions or causing constipation, as would opium.

In **cardiac palpitation**, as well as in some cases associated with **vertigo**, *cannabis indica* has been used with asserted good results (Sée).

The efficiency of the drug as an **aphrodisiac** appears, at least in western races, to have been overestimated. In moderate doses the effect of the drug is said to be rather a sedative one. In case of hyperirritability of the genital mechanism in the male, with resulting functional impotence due to premature discharge, *cannabis indica*, by diminishing peripheral sensibility, tends to promote normal completion of the procreative act (Goodwin).

In the treatment of **sexual atony** in the female the following combination has been recommended:—

℞ *Extracti cannabis indica*,  
*Extracti nucis vomica* .....āā gr. xxx (2 Gm.).  
*Extracti aloes* .... gr. vij (0.5 Gm.).

Ft. in pil. no. c.

Sig.: One pill three times a day.

For **impotence**:—

℞ *Ext. cannabis indica*,  
*Ext. nucis vomica* ..āā gr. xv (1 Gm.).  
*Ext. ergotæ (aqu.)* ..... ʒj (4 Gm.).

Ft. in pil. no. xxx.

Sig.: One pill morning and evening.

Da Costa (quoted by V. Robinson, Med. Rev. of Rev., March, 1912).

*Cannabis indica* is a constituent of many preparations employed externally in the treatment of **corns**, including the *Collodium salicylatum compositum* of the National Formulary. In **ichthyosis hystrix** Van Harlingen applies the following preparation:—

℞ *Acidi salicylici* ..... ʒss.  
*Ext. cannabis indica* .. gr. x.  
*Collodii* ..... fʒj—M.

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**CANTHARIDES.**—The dried bodies of the *Cantharis vesicatoria*, the blister-beetle, or “Spanish fly,” a coleopterous insect, also called *lytta*, is collected in Russia, Sicily, and Hungary, but is also found in Spain, France, Germany, and other parts of Europe. Representatives are found in various parts of the world, notably in the Levant and eastward, in Senegal, Southern and Central America, and in Chile. The insect is about an inch long, perhaps one-fourth inch broad, flattish, cylindrical, with filiform antennæ; it is black in the upper part, with long wing-cases, and has large, membranous, transparent, brownish wings; elsewhere the insect is of a shining, coppery-green hue. The powder is grayish or blackish brown, containing green, shining particles, with strong, disagreeable odor and acrid taste, and is soluble in alcohol. Cantharides is often adulterated, especially when powdered, with other beetles and ground gum-resin euphorbium.

The active principle of cantharides, discovered by Robiquet, is termed *cantharidin*. It occurs as scaly crystals,



which are inodorous and tasteless. Though insoluble in water and practically so in alcohol when in its pure state, cantharidin, when in organic combination as it is in the Spanish flies, yields its virtues to these agents.

#### PREPARATIONS AND DOSES.

—Although the Pharmacopeia includes the powder of cantharides among the official preparations *Cantharis*, U. S. P., average dose,  $\frac{1}{2}$  grain (0.03 Gm.), it is little used. It contains 0.6 per cent. of cantharidin. The preparations in general use are:—

*Tinctura cantharidis* (tincture of cantharides), prepared with 10 per cent. of the powder. Dose, 1 to 5 minims (0.06 to 0.3 c.c.).

*Ceratum cantharidis* (cantharidal cerate, fly-blister) is composed of cantharides, 350 Gm. ( $11\frac{1}{3}$  ounces); oil of turpentine, 150 c.c. (5 ounces); yellow wax, 175 Gm. (6 ounces); rosin, 175 Gm. (6 ounces); lard, 200 Gm. ( $6\frac{1}{2}$  ounces). Used externally.

*Collodium cantharidatum* (cantharidal collodium; blistering collodium) is made from cantharides, 60 Gm. (2 ounces); glacial acetic acid, 5 c.c. (80 minims); flexible collodion, 85 Gm. (3 ounces), and acetone, enough to make 100 Gm. ( $3\frac{1}{3}$  ounces). Used externally.

*Emplastrum picis cantharidum* (cantharidal pitch plaster), though not official, is at times used. It is composed of Barbadoes pitch, to which 8 per cent. of the above-described cantharidal cerate is added.

#### PHYSIOLOGICAL ACTION.—

In therapeutic doses cantharides tends to stimulate cardiovascular activity, increasing the power of the cardiac contractions and raising the blood-pressure. This is probably due to stimulation of the vasomotor

centers. The temperature may also be somewhat raised when full doses are taken. The main action of cantharides is upon the genitourinary system, therapeutic doses producing free diuresis and a tendency to enhance sexual desire, reaching in man, if the dose is large, to priapism and seminal emissions, and, in women, to erotic excitement, adventitious menstruation, and even abortion. Ten minims (0.6 c.c.) of the tincture sometimes suffice to produce violent sexual excitement in either sex, while large doses will produce the opposite effect. The sensitiveness to cantharides varies greatly in different individuals.

It is important to use extreme accuracy in fixing the dose of cantharidin, for, whereas there are some patients in whom the administration of  $\frac{1}{200}$  of a milligram (0.00002 Gm.) will cause albuminuria, there are others who easily support seven times this dose, given thrice a week, over a period of many years.

The tincture of cantharides, even if prepared with the greatest care, cannot be regarded as anything but most uncertain in composition, and this is due to the fact that the active principle in cantharides varies between 0.3 and 0.6 per cent. It is obvious, therefore, that some tinctures may have double the strength of others. Unfortunately, cantharidin is insoluble in water; the writer finally overcame the difficulty by administering the drug in tinct. cort. aurant. in the proportion of 0.2 cantharidin to 1000 of the tincture. In practice this artificial tincture was not used in the shape of drops, but was measured by means of the Pravaz syringe. One c.c. (16 minims) of the liquid contained, therefore, 0.0002 gram, that is, 2 decimilligrams of cantharidin. As a rule, 0.5 c.c. (8 minims) sufficed, and the writer has never administered more than 0.75 c.c. (12 minims) at one dose. The tincture should be taken dissolved in a liqueur glassful of

water. Oscar Liebreich (Brit. Med. Jour., Oct. 18, 1902).

*Locally* applied, cantharides acts slowly but powerfully as an irritant, producing not only vesication if left too long, but also tissue necrosis. This is especially apt to be the case in children, and in women whose skin is very white and tender. Redness of the skin with tingling and burning are followed by the formation of vesicles, which rapidly coalesce, causing a vesicle filled with blood-serum. This, the *vesicatory* action of cantharides, often used to produce counter-irritation, sometimes gives rise to albuminuria, acute uremia (Ferrand), and other toxic phenomena through absorption. The counterirritation is exercised reflexly, mainly through the vasomotor system. Zuelzer found that it produced ischemia of the deeper tissues, the lungs, for example, when the vesicatory is applied to the chest.

**UNTOWARD EFFECTS AND POISONING.**—When excessive doses of cantharides are administered all the foregoing symptoms may be exaggerated. The specific action of the drug on the genitourinary system shows itself by strangury, frequent desire to micturate, bloody urine, and violent pain in the bladder and loins. There is often violent sexual excitement, accompanied by painful priapism and frequent emissions. Abortion may be caused. The external genitalia may become inflamed and swollen and even gangrenous.

When a poisonous dose of a strong solution or of the powder itself is taken, there occurs, after a few minutes, violent burning pain in the mouth, pharynx, esophagus, and epigastrium, soon followed by more or

less violent salivation, vomiting, and purging. If a toxic dose of the powder has been taken, small, greenish specks are found in the vomitus. The latter and the stools are often bloody. Severe tenesmus is a constant symptom in such cases. Violent delirium and convulsions occasionally occur.

When the toxic dose is very large, the phenomena witnessed may include no sign of erethism and be entirely those of collapse. In such cases the pulse becomes rapid and weak, the arterial pressure falls, and the early prostration rapidly deepens into insensibility, coma, and death. One ounce (31 Gm.) of the tincture; 24 grains (1.6 Gm.) of the powder (Stillé), and cantharidal blisters (Huchard), respectively, have caused death.

Case in which, instead of a blister the size of a shilling being applied, the whole of the surface outlined (measuring 7 by  $2\frac{3}{4}$  inches) was painted over with liquor epispasticus (B. P.). One hour later the first symptoms of strangury appeared—viz., an urgent desire to micturate, associated with the passage of blood-stained urine in small quantities and at frequent intervals of about five minutes. A slight degree of headache was noted, the pulse ran up to 120 a minute, and the patient broke out into a profuse perspiration. The pain, which was referred to the distal end of the penis, was intense. The abdomen was soft and yielding and there was a marked absence of tenderness in the loins. A fourth of a grain (0.016 Gm.) of morphine gave relief from pain. The amount of urine passed during the first twenty-four hours was 28 ounces. The specific gravity was 1019 and the reaction to litmus proved acid. Blood and albumin were present, the latter being estimated at 7 Gm. ( $1\frac{3}{4}$  drams) per liter. The microscopic sediment

consisted largely of mucus with numerous red and white blood-corpuscles and kidney cells (large round cells, with vesicular nuclei and granular protoplasm twice to four times the diameter of a red corpuscle).

On the following day the patient passed a normal quantity of urine (51 ounces), but still complained of burning pain with micturition. J. S. Avery (Lancet, Sept. 12, 1908).

Case of pleurisy in which a piece of plaster (*emplastrum cantharidis*, B. P.), measuring  $5\frac{1}{2}$  inches by  $4\frac{1}{2}$  inches, was applied to the chest wall below and to the outer side of the left nipple. Thirteen hours afterward the first symptoms appeared. The patient felt a desire to pass urine every hour or so and could not keep (*i.e.*, retain) it for a longer period. Pain was experienced at the end of the penis when the act was nearing completion; the urine voided was the color of beet-root water. Headache developed in conjunction with the other symptoms, but there was neither vomiting nor purging; indeed, it appears that for the first forty-eight hours the bowels remained inactive.

On admission, on Sunday, July 26th, the physical signs indicative of disease were those of pleurisy with effusion on the left side. There was a raw surface measuring  $5\frac{1}{2}$  inches by  $4\frac{1}{2}$  inches below and to the outer surface of the nipple. The temperature was  $102^{\circ}$  F., pulse 106, and respirations 39 per minute. The belly wall was not rigid and there was a complete absence of abdominal pain and tenderness. The patient apparently did *not* experience pain in the region of the kidneys. There was no undue frequency of micturition though a good deal of pain of a burning nature was present just within the orifice of the urethra toward the end of the act of micturition. The urine was loaded with amorphous urates and red cells, and yielded, after careful filtration, a well-defined cloud of albumin. The specific gravity of the filtered urine was 1028, and it was

acid in its reaction to litmus paper. Currie (cited by J. Stanley Avery, Lancet, Oct. 10, 1908).

Case of cantharides poisoning in which a most marked erythremia (10 million) appeared shortly after the incidence of the poisoning. This continued though to a somewhat less degree, for a number of days. The patient's temperature was subnormal in the beginning but later became normal. There was slight acceleration in the pulse rate. Recovery ensued in 20 days. Lipsitz and Cross (Arch. of Internal Med., Dec., 1917).

While the disorders produced are, as a rule, most prominent in the genitourinary system, other systems—the digestive, nervous, cutaneous, etc.—may receive the brunt of the morbid effects of the drug. Acute nephritis with anasarca, dyspnea, convulsions, and uremic amaurosis, with complete anuria, have been observed by Huchard after the application of a small blister.

Case in which a small bald area on the head was painted with *liquor vesicatorius* (B. P.) twice in eight days. About eight days after the second application intense edema of the scalp, face, neck, and upper chest set in. Soon there occurred a universal exanthem and hematuria. Then the hairs of the entire body and the nails fell out. After nine months the nails grew again, but the hair did not. Barton (Lancet, Oct. 24, 1905).

Cantharis does not cause a production of new red cells, but merely a condensation of the blood through the loss of water in the process of elimination by the kidneys. Morgulis and Muirhead (Arch. of Internal Med., Feb. 15, 1919).

**TREATMENT OF CANTHARIDAL POISONING.**—There is no known antidote for cantharides, and toxic cases must be treated in consonance with the indications afforded by each individual case. Free wash-

ing out of the stomach with warm water, employing the stomach pump or tube, or the promotion of free vomiting is imperative. Demulcents such as albumin, mucilage, or milk and lime water are very helpful after washing of the stomach and emesis have rid it of the poison. Bland oils have been suggested, but these are dangerous, since they are apt to separate the cantharidin, which is very soluble therein. Free enemas also aid in carrying away any of the toxic which may have reached the colon. Morphine hypodermically or laudanum per rectum are always demanded to allay the excruciating suffering and the severe strangury. The cautious use of anesthetics sometimes becomes imperative. Camphor monobromate often alleviates the most distressing symptoms in mild cases, and bromides become necessary when there is a tendency to delirium and convulsions.

To allay the subsequent gastrointestinal irritability, bismuth subcarbonate is very efficient, while cocaine hydrochlorate may be added in severe cases of this class.

**THERAPEUTICS.**—Cantharides so frequently caused untoward phenomena, particularly in the urinary system, that its preparations are but little used internally nowadays, many other and safer drugs being available for the treatment of disorders in which they were at one time employed. At best their use may be resorted to when other resources fail in conditions of the genitourinary apparatus attended by atony. Thus, when **enuresis** or **diurnal incontinence** occurs as a result of atony of the sphincters or of the bladder, especially in women, or **gleet**, **spermatorrhea**, or

**prostatorrhea** are associated with general debility; or when **impotence** is the result of old age, masturbation, or sexual excesses; or **menorrhagia** or **amenorrhea** persists in debilitated women, a small dose of the tincture, three times a day, may prove efficient when appropriate remedies are simultaneously employed to offset the cause of the general adynamia. Small doses have also been recommended in **chronic cystitis**; but here also cantharides should be tried only after other remedies have been found ineffectual.

**Local Uses.**—It is principally as a revulsive that cantharides, or fly-blister, is still occasionally employed. This requires, however, considerable care. After a period varying with the sensitiveness of the patient's skin, a burning sensation is experienced and the skin becomes red. In six to eight hours the superficial layers of the epidermis become detached and transparent bullæ are formed, which soon coalesce, forming a blister the size of the area covered by the vesicant, the underlying rete Malpighii being the seat of an acute inflammation. When the vesicant is left on the skin beyond this stage, ulceration occurs. Moreover, as the serum in the blister gradually takes up cantharidin, the latter is absorbed by the vessels of the rete, giving rise to untoward phenomena—beginning with frequent urination, soon followed by strangury and pain in the loins—if the vesicant is left on beyond the blister-forming stage. In women, children, or other individuals having a tender skin, this stage may come on almost any time after rubefaction has begun. All cases in which cantharidal vesication is resorted to should, therefore, be

closely watched. Albuminuria and acute uremia in the aged or debilitated and death in infants from acute nephritis have occurred owing to neglect of precautions.

Additional drawbacks in the use of cantharidal vesication are afforded by the fact that a broad surface is created, which exposes the patient to streptococcic and other infections. Erysipelas, furuncles, and anthrax have thus been caused,—a fact which has awakened in the minds of most clinicians considerable doubt as to whether the benefit derived from this agent is not more than offset by its many dangers.

The precautions that are imperatively necessary when a fly-blister is employed are: 1. To remove it as soon as bullæ begin to form; this should be done carefully lest particles of cantharides remain and continue its vesicating action. 2. A warm flax-seed-meal poultice, the surface of which has been sprayed with camphor water, as a mild antiseptic, is then applied. 3. The vesicle forming as it would have if the fly-blister had been left on, it should be aspirated with an aseptized hypodermic needle to remove the serum containing cantharidin, and thus obviate absorption complications. Finally, an aseptic dressing should be applied and carefully watched to prevent contamination.

The disorders in which blisters have been advocated are those in which the deeper organs are the seat of an acute inflammatory process or at least active congestion, the object being to produce ischemia, as in the congestive stages of **pneumonia, pleurisy, pericarditis, pancreatitis, cerebritis, meningitis, otitis media, ovaritis, metritis,**

**periostitis, and synovitis.** While in thoracic and abdominal disorders the blister may be applied over the diseased organ, the size of the vesicant being larger for the lungs than for the other organs, inflammatory disorders of the head are best treated by applying it to the nape of the neck, and in meningeal disorders on one side of the vertebræ, to avoid ulceration over the tips of the processes which rest on the bed. Blisters are also of service when the usual measures fail to arrest **obstinate vomiting,** and the acute suffering of **gastralgia.** The cantharidal plaster applied in strips over the affected nerve is often very efficient as an adjunct in the treatment of **intercostal and brachial neuralgia** and in **sciatica.**

The local application of blisters to patches of **tinea tonsurans** and **alopecia areata** is sometimes efficacious, but the area covered in each case should be small. The tincture of cantharides is an efficient component of lotions used for the treatment of **alopecia** and **dandruff** or **pityriasis capitis.**

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**CAPSICUM, U. S.,** or cayenne pepper, is the fruit of the *Capsicum fastigiatum*, a plant of the natural order Solanaceæ, native to tropical Africa and South America. It occurs in long, scarlet pods, and has an intensely hot taste and a peculiar odor. The two latter attributes are due to a volatile alkaloid, capsin ( $C_9H_{14}O_2$ ), which is the active principle and irritant to the skin and mucous membranes. Capsicum is a thick, red liquid. It contains a resin and a fixed oil.

#### **PREPARATIONS AND DOSES:**

*Powdered capsicum.* Dose 1 to 5 gr. (0.06 to 0.3).

*Oleoresin (oleoresina capsici, U. S.).* Dose 1 to 5 minims (0.06 to 0.30).

*Fluidextract (fluidextractum capsici).* Dose 5 minims to a dram (0.30 to 4). No longer official.

*Tincture (tinctura capsici, U. S. and B. P.).* contains 5 per cent. of capsicum. Dose 10 minims to a dram (0.6 to 4).

*Capsicum liniment (linimentum capsici),* 1 in 10, used for chest affections, rheumatism, etc.

*Capsicum plaster (emplastrum capsici),* for external application.

**PHYSIOLOGICAL ACTION.**—Capsicum is irritant to the skin and mucous membranes, causing first redness and eventually vesication. Internally in medicinal doses it produces a sense of warmth in the stomach, stimulates the secretions, thus promoting appetite and digestion, and by stimulating the bowel produces easy and copious passages. It is diaphoretic, diuretic, and decidedly aphrodisiac. The heart and nervous system are stimulated, but in repeated doses the drug is slightly narcotic. Capsicum exerts a vasoconstrictor effect on the vessels by stimulating the muscular coats, either directly or through the vasomotor nerves. In large doses it produces gastritis, acute nephritis, and strangury.

**THERAPEUTIC USES.**—Capsicum is used as a condiment, carminative, gastric stimulant, and rubefacient. In **atonic dyspepsia** capsicum is an excellent stomachic tonic, especially if the condition is due to **alcoholism**. In cases of **mania a potu** and **delirium tremens** it promotes sleep and desire for food, and is a good substitute for alcohol and opium in treating those addicted to their use. In acute alcoholism the gastric mucous membrane may be in an irritated condition and it will be best not to give capsicum for the first few days. In **flatulence** and **colic** of nervous women it is useful. It gives good results in cases of functional **impotence**, **spermatorrhoea**, **prostatorrhoea**, and **chronic cystitis**, and in chronic parenchymatous nephritis it will reduce the albumin in the urine, but should be avoided in this disease. Given internally and a plaster applied over the loins externally the drug will relieve **renal congestion** with persistent lumbar pain and slight albuminuria.

In **tonsillitis** and **relaxed uvula**, equal parts of the tincture and glycerin or equal parts of the tincture and honey are a useful application. In **lumbago** or **muscular rheumatism** anywhere, the mustard plaster (**emplastrum capsici**) is valuable and acts as a moderate counterirritant, seldom producing a blister. Applied to the nape of the neck, it will relieve **headache**. The **pruritus** and pain of **chilblains** and **rheumatic joints** may be quickly relieved by applying a plaster of absorbent paper which has been saturated in a strong tincture of capsicum, but this method is not to be used if the skin is broken. W.

**CARBOLIC ACID.** See PHENOL.

**CARBON MONOXIDE POISONING.** See GASES, POISONING BY.

**CARBUNCLE.** See SKIN, SURGICAL DISEASES OF.

**CARCINOMA.** See CANCER.

**CARDIOSPASM.** See STOMACH, DISEASES OF.

**CARRON OIL.** See CALCIUM.

**CASCARA SAGRADA.**—*Rhamnus purshiana* (cascara sagrada, Br., Fr. Cod.; chittim-wood bark; bearberry; bearwood; sacred bark, E.) is the dried bark of *Rhamnus purshiana* D. C. (fam., Rhamnaceæ), collected at least one year before being used (U. S. P.)

Cascara sagrada is official in all the more important pharmacopœias, except the German. The plant is a large shrub or small tree found in the northwestern United States and adjacent British America, extending south to northern California. It occurs in short quills mostly  $\frac{1}{2}$  to 1 inch (1 to 2.5 cm.) in diameter, or in curved pieces of the same about  $\frac{1}{2}$  to  $\frac{3}{8}$  inch (2 to 5 mm.) thick; the dried quills of bark are now mostly broken up and packed tightly under pressure before being marketed.

Cascara sagrada contains much resin and emodin ( $C_{15}H_{10}O_5$ ), frangulin ( $C_{21}H_{20}O_6$ ), 3 resins, tannin, purshianin, cascacin, chrysarobin, chrysophanic acid, glucose, a fixed oil, a little strongly odorous,

yellow-green, volatile oil, rhamnol (apparently identical with quebrachol), a non-laxative hydrolytic enzyme, and a substance yielding syringic acid on treatment with acids. Jowett, in 1904, showed that "cascarin" and "purshianin," reported by previous investigators, were impure emodin, and that emodin is not active. Purshianin probably contains the active constituent, as it was found laxative in  $\frac{1}{16}$  grain (0.013 Gm.) doses. The active principle is probably a derivative of a glucoside present in the bark. The bitter taste appears to be due to the enzyme or ferment discovered by Meier and Weber.

**PREPARATIONS and DOSES.**—The official preparations are as follows:—

*Cascara sagrada*, U. S. P. (the crude drug). Dose, 15 to 30 grains (1 to 2 Gm.).

*Extractum cascarae sagradae*, U. S. P. (extract of cascara sagrada). Dose, 2 to 10 grains (0.13 to 0.65 Gm.).

*Fluidextractum cascarae sagradae*, U. S. P. (fluidextract of cascara sagrada). Dose, 15 minims (1 c.c.).

*Fluidextractum cascarae sagradae aromaticum*, U. S. P. (aromatic fluidextract of cascara sagrada). Dose, 30 minims (2 c.c.).

Unofficial preparations much used are:—

Elixir cascarae sagradae, N. F. (elixir of cascara sagrada). Dose, 1 fluidram (4 c.c.), representing 30 grains (2 Gm.) cascara sagrada.

Elixir cascarae sagradae compositum, N. F. (compound elixir of cascara sagrada, containing senna, juglans-butternut, and cascara sagrada with aromatics). Dose, 1 fluidram (4 c.c.).

Fluidextractum rhamni purshianae alkalinum, N. F. III (bitterless fluidextract of cascara sagrada). Dose, 15 minims, (1 c.c.).

**PHYSIOLOGICAL ACTION.**—Cascara sagrada increases the secretions of the gastrointestinal canal, and because of its bitterness acts as a tonic, improving the appetite and digestion and preventing the constipation which usually follows the use of similar drugs. The tonic action of cascara is also exerted upon the musculature of the bowels, thereby increasing peristalsis; so marked are these effects that the dose may be gradually diminished, and its use finally discontinued without the reappearance of the constipation. In

a number of clinical cases Milnes Hey has observed a sensible diuretic effect. Cascarin, which occurs in prismatic needles of a variable orange color, devoid of odor or taste, appears to have slight cholagogue properties; it causes an easy evacuation of the bowels with semiacid stools, without griping, does not excite nausea nor diarrhœa, nor is its use followed by constipation; it may be given in doses of  $1\frac{1}{2}$  to 15 grains (0.1 to 1.0 Gm.). The fresh bark has decided emetic properties, causing nausea and vomiting; these properties are lost by keeping the bark for one year. Large doses may produce irritation of the bowel and intestinal catarrh.

**UNTOWARD EFFECTS.**—R. O. Cotter reported 2 cases in which cascara sagrada in ordinary doses produced very exhausting purging, with great prostration and feebleness, lasting several days. C. M. Fenn reported several cases showing that griping, pain, vomiting, bloody stools, and abdominal tenderness may be caused by the drug. One case of insanity he believed to have been of reflex nature, arising from the gastrointestinal irritation caused by the continued use of the drug. In another patient, dying of cerebral anemia, there were a number of ecchymotic patches on the stomach, which the writer ascribed to excessive use of cascara. G. E. Greene recalled 3 patients in which the fluidextract produced vomiting and griping, but in whom the tasteless preparations were not only well borne but effectual.

**THERAPEUTICS.**—Cascara is, and should be used only as, a tonic laxative and never as a cathartic or purge. Through neglect of this have arisen the numerous cases in which untoward effects have been observed. Its chief use is in habitual or chronic constipation. To obtain the best results it should be given in small doses at frequent intervals—at least three times a day, thereby securing a continuous impression on the digestive tract. The initial dose should be small, gradually increased until regular evacuations are established, then gradually diminished, and finally discontinued. It is also a valuable hepatic tonic in congested liver and duodenal catarrh. In atony of the bowels, it may be used in combination with ber-

beris; in **anemia** and **chlorosis** it is best given with some ferruginous preparation, as the citrate of iron and ammonia. With the salicylates, *cimicifuga*, or some other potent remedy, it will be found useful in **rheumatism**. It is a useful adjuvant to other diuretics and cathartics. In **cholelithiasis** and **appendicitis**, diseases of bacterial origin, the occurrence being favored by deficient action of the bowel, cascara will, by inducing regular action, act as a prophylactic. In **rheumatoid arthritis**, due to absorption of toxic products which have been retained in the intestine, cascara will also exert a prophylactic action by establishing regular and satisfactory evacuations. In **sciatica** its use has been followed by relief and final cure. W.

### CASEIN SILVER. See SILVER.

**CASTOR OIL** (*oleum ricini*) is a fixed oil expressed from the seeds or beans of *Ricinus communis* or *Palmi christi* (fam. Euphorbiacæ), a plant native to India, but cultivated in America, where it grows to a height of five feet and produces pods which contain three seeds each. These seeds are ovoid, gray-marbled or striped, shiny, and from them the oil is derived. The oil is viscid, transparent, and colorless, with a peculiar, slightly acrid taste and odor, is neutral in reaction, and has a specific gravity of 0.95 to 0.97. It is soluble in an equal weight of alcohol and becomes solid at a temperature of  $-0.4^{\circ}$  F. It contains ricinoleic acid ( $C_{18}H_{34}O_3$ ), glycerin, and small quantities of palmitin, stearin, cholesterol, and a resin.

### ADMINISTRATION AND DOSE.—

The dose of castor oil for an infant is 1 to 2 drams (4 to 8 c.c.), and for adults from a half to an ounce (15 to 30 c.c.). As an alternative, in chronic dysentery, for example, it is also given in doses of 10 minims (0.6 c.c.) three times a day. Applied with friction to the abdomen of children it frequently purges.

The taste and odor of castor oil are objectionable to most people and various means are taken to overcome them. The odor may be masked by the oil of bitter almonds. So-called castor-oil sandwiches may be employed by putting whisky, thick

cream, lemon juice, or peppermint water into a glass, gently pouring in the oil, and topping off with a little more of the first fluid. A mouthful of milk is then taken and the sandwich taken at one gulp. The eating of some strong peppermint drops before and after taking is helpful. Foaming beer is a good vehicle, or the oil may be taken in sarsaparilla soda water, or mixed with an equal quantity of glycerin, which increases its purgative effect, and a few drops of an aromatic oil. A little sodium bicarbonate is also said to help the purgative action. Soft capsules containing from a half to a dram (2 to 4 c.c.) are easily procured and are the best way of taking the oil. They should be dipped in water to facilitate swallowing, and enough taken to make up the required dose. Emulsions are not a success and probably only detract from the efficiency of the oil. Castor oil is one of the ingredients of *colodium flexile*, 3 per cent.

**PHYSIOLOGICAL ACTION.**—Applied externally, castor oil is bland and un-irritating. Taken internally, it passes through the stomach unchanged, but in the duodenum is broken up by the pancreatic juice into ricinoleic acid and other substances. This acid mildly irritates the bowel, stimulating the muscular coat and glands, thus increasing peristalsis and secretory activity, and so producing purgation.

Probably the oily residue lubricates the bowel also, thus helping the purgative action. The liver is not affected, but the moderate duodenal irritation may indirectly slightly increase the flow of bile. The ricinoleic acid, being absorbed, enters the blood and body secretions, and in a nursing mother the suckling will be purged. Castor oil is a simple purge and acts in from four to six hours. The purging is without pain or tenesmus, is not excessive, and is followed by a sedative action on the bowel. Applied to the mammary glands, a poultice of the leaves is said to possess galactogogic properties.

**THERAPEUTIC USES.**—Castor oil is the least irritating of the purges and because of its mild action can be used with safety when other purges would be dangerous, as in the constipation of typhoid fever. In children who have eaten un-



wisely it is useful to unload the bowels, and in the **diarrheas of children** it is well to begin treatment with a good house-cleaning by this agent. Indeed, in many cases this will be all the treatment required, as the removal of the irritating material from the bowel and the soothing effect of the oil will often check the diarrhea without further treatment. During or following **pregnancy**, or after operations, it is the purge of choice. In **hemorrhoids**, pelvic inflammatory conditions, **cystitis**, **calculi**, **gonorrhea**, or **stricture** it is valuable. In **dyentery** due to irritation it will sweep out the pathogenic material and soothe the bowel, and its secondary constipating effect will tend to stop the excessive evacuations. Ten to 20 drops (0.6 to 1.2 c.c.) of laudanum should be added to help relieve the pain and tenesmus, and if the patient is depressed and the pulse weak 5 minims (0.3 c.c.) of ol. terebinthinae may also be added.

Castor oil should not be used for chronic constipation, as after it has acted the bowels become more tightly locked than before. If used constantly the oil tends to produce hemorrhoids by congesting the hemorrhoidal vessels. The purer the sample employed, the milder the purgation.

W.

**CASTS IN THE URINE.**—Tube casts are believed to consist of a coagulable substance closely allied to proteids which enters the renal tubules through lesions of their walls. Any free or partly detached products of the tubules become adherent to the basis substance. A cast consisting solely of the latter is called a *hyaline cast*. Addition of epithelium or blood-corpuscles forms *epithelial* or *blood-casts*. Addition of disintegrated tissue matter forms *granular casts*. Similarly, *fatty*, *bacterial*, and *pus-casts* may be formed. One form of hyaline cast, usually large, occasionally gives an amyloid reaction with methyl-violet and Lugol's solutions. The edges may be indented, but their surface is smooth. This is the so-called *waxy cast*, found in all forms of nephritis, irrespective of amyloid renal disease. The amyloid reaction probably indicates a degenerative change in the cast itself.

Long, wavy structures, often dividing

and subdividing at their ends, are the so-called *cylindroids* of Thomas. They are not characteristic of renal disease, but rather of an irritation of the lower urinary tract which has extended up to the kidneys.

**Detection.**—Casts are collected for examination by allowing the urine to stand for 24 hours, or better, by use of the centrifuge for 2 or 3 minutes. A portion of the sediment placed on a slide is examined with the  $\frac{1}{4}$ -inch objective in a clear, but not too strong light. Casts may be stained, as recommended by H. B. Erdman, by treating for 3 minutes with 5 per cent. mercuric chloride solution, washing in water, and applying for 5 minutes a fresh mixture of 0.3 per cent. methylene blue and 0.02 per cent. fuchsin aqueous solutions. The preparation is then washed, and may be dried and mounted in balsam. According to Heitzmann, actual identification of cast-like structures as tube-casts is justified only in the presence of other evidences of a pathologic condition, such as red corpuscles, leucocytes, or pus-corpuscles and epithelia from the uriniferous tubules.

S.

**CATALEPSY, CATATONIA, AND NARCOLEPSY.**—Catalepsy is the name given to a state of which the most striking feature is that a subject's unsupported limb will remain in whatever position it is placed without falling by gravity. To a mask-like immobility of the face the same term may be applied. Formerly believed an autonomous disease, it is now known to be merely a manner of reaction of the nervous system, provokable in several different ways; that is to say, it is only a *symptom* which may be expressed in the course of divers diseases.

Catalepsy may be *total* or *partial*, and either may be *complete* or *incomplete*.

**SYMPTOMS.**—*Flexibilitas cerea* was the expressive name used to denote the ready plasticity which usually allowed the operator to move

the patient's limbs without resistance. A tonic muscular state, however, very hard to overcome, has been presented in some cases. A usual characteristic of the cataleptic is an apparent insensibility, not only of the skin and deep tissues, but of the organs of special sensations; so that inaccessibility to all stimulation of the organs of sense was conspicuous in early descriptions of the disorder. Joined to the motor and sensory paralysis was an apparently complete absence of spontaneity and the exercise of will. The person appears like an automaton.

What has been termed "catatonic hirntod" or brain death, may be present instead of true catalepsy. It is a psychosis of acute onset followed by death within 15 days and showing at autopsy neither gross nor microscopic visceral alterations of sufficient intensity to be regarded as factors in the disease or cause of death. Clinically the diagnosis is not definite on account of the short time of observation and the condition of the patient, but the limited data place it probably as a case of dementia precox of the katatonic form. Orton (Amer. Jour. of Insanity, Apr., 1913).

In the cases which may be called total and complete, the patient may be believed dead; for not only are the limbs inert, the eyes staring or half-closed and the pupils dilated, with drooping jaw, and the skin cold and pale; but their respiratory movements cease, the pulse is impalpable, and swallowing is not effected. Only the heart can be felt to beat faintly, for even the reflexes may be entirely suppressed; although most observers find the corneal reflex; and the rectal temperature approximates normal.

Case in a Motala Brahmin girl aged 18 years who had just recovered from

remittent fever, and was being treated for anemia and debility. She was progressing fairly well, when one day at about 2 P.M., while sitting with her friends, she felt drowsy, and while going to her bedroom fell down and became unconscious. Her friends and relations, having tried in vain to rouse her, thought that she was dead. When seen at about 9 P.M. she was lying on her back, with her limbs stretched and stiff. Her face was calm. The pulse and respirations were imperceptible. Temperature subnormal. Conjunctival reflex absent. Cotton held to the nostrils or mirror to the mouth did not show signs of respiration. Heart and lungs apparently seemed to have stopped their functions.

The writer tried to rouse her by holding ammonia to the nostrils, splashing the face with cold water, tickling the Schneiderian membrane, and lastly by applying faradization, but to no purpose. The *flexibilitas cerea* was found to be present. Her forearm was flexed on the arm, and it remained in that position without support; both the forearms could remain in any position in which they were placed. The writer gave 5 minims (0.3 c.c.) of ether hypodermically and repeated it after half an hour. Soon after, the temperature rose to normal and feeble beats of the pulse could be felt. The dose was repeated after an hour, when the heart began to throb steadily. The respirations became free and regular. The patient opened her eyes. A. S. Malva (Indian Med. Rec., July, 1908).

It is often surprising to find what a clear appreciation and understanding of what has been going on are displayed by persons rousing from a period of catatonia during which they lay like a lifeless statue with closed eyes. As a rule, however, the period of stupor is a blank in the memory. Wimmer (Hospitalstidende, May 30, 1917).

So complete may be the suspension of vital activity that a case is re-

ported to have survived after twenty minutes' immersion in water into which she had fallen during an epileptic fit. Perhaps one of the most remarkable cases reported is that of the *dormeuse* of Thenelles, whom many physicians observed during her twenty years of catalepsy.

[The young girl known in literature as "the sleeper of Thenelles" was attacked with violent hysterical fits during twenty-four hours. After the last one the patient remained in a lethargic state until 1887. This lethargy was interrupted every month or so by convulsive attacks in which the patient tore her face and chest with her nails. The attacks ended by abundant salivation or by profound perspiration, but the loss of consciousness was said to be always complete. There was general anesthesia from the beginning and a hysterogenetic zone over the sternum, which disappeared after a hemorrhage from the nose and mouth.

In 1887 the patient was very thin, with scaphoid abdomen; the features were expressionless. On lifting the eyelids suddenly the eyes appeared normal, the pupils were slightly contracted, but the lightest touch caused a convulsion, and even a breath would cause the eyelids to tremble. The breathing was calm, light, and slow. The pulse was regular, though rather rapid. The temperature  $37^{\circ}$  to  $37.8^{\circ}$  C. There was complete anesthesia of the skin and mucous membranes. Sometimes the introduction of the esophageal sound or the falling of drops of liquid into the mouth produced a violent spasm.

The sensibility returned under the influence of hypodermic injections of sulphate of atropine. For a week or more these injections were given daily, during which time the sensibility returned as high as the trunk. Complete anesthesia returned when the injections ceased.

The head was fixed and slightly bent forward, the neck muscles being in contraction. When the arm was lifted it remained in that position, stiff even to the fingers, and this attitude was kept for hours.

The patellar reflexes were much exag-

gerated, and raising the foot caused ankle clonus, but of the irregular type, not indicative of pyramidal-tract disease. During these provoked excitements the face flushed and the pulse became more rapid. The convulsions always began on the right side, even although provoked, for example, by percussing the left patellar tendon or raising the left foot.

The convulsive attacks disappeared at the beginning of 1887, and did not reappear until the end. There was slight jaundice. It was most pronounced in 1896, without any appreciable shrinking of the liver dullness. The temperature was raised a few tenths after the convulsions were provoked.

In 1902 a small tumor appeared on the forearm, and during the introduction of a probe the patient shrank back. In 1903 a frequent cough was noticed, and another swelling like that on the forearm was seen on the right foot.

A few days after the appearance of the cough, there was a sudden attack of grand hysteria resembling those at the beginning of the illness. These attacks ended in a few minutes, but began again in about a quarter of an hour and continued at intervals. These convulsions were followed by relaxation of the limbs, the eyes opened, and the jaw alone remained contracted. Two days later the convulsions ceased, the patient opened her eyes, put her hand up to them as though to push aside a veil, and appeared to hear and seek to recover herself.

The next day she was still more awake. She opened her eyes when ordered, appeared to see, and passed her hand several times over her eyelids. When pinched on the arm and on being asked what had been done, she answered in a weak but clear voice, "You pinched me."

From this time the somnambulism and the accompanying symptoms completely ceased. The patient groaned and raised herself several times in bed. When asked if she was in pain she pointed to her chest. Auscultation showed râles of both lungs, and she died on May 28, 1903, without again losing consciousness, asking and answering questions. The temperature after the awakening was constantly below normal.

Voisin also saw this patient during her long sleep, and proved that she was not altogether unconscious by using words that made her blush.

Farez, too, found that she resisted strongly attempts to open her lips, open her eyelids, or flex or extend the limbs. He believed, too, that the contractures, tremors, and hysterogenetic zones were due to the suggestions of the procedures to which she had been submitted by different examiners.]

The *onset* may be sudden or gradual. The state may be dramatic in its manifestations, or may require an experienced clinician to ascertain it. Contrary to the general belief, the latter condition is by far the more usual, although less often reported in literature (Latron). It may come as a bolt from the blue without preceding signs, or it may be preceded by headache, nausea, hiccough, dizziness or emotionalism, and, of course, by the symptoms of whatever condition in the course of which the catalepsy is developed, as, for example, typhoid fever, uremia, alcoholism, dementia præcox, hysteria, etc.

The cataleptic state is sometimes very brief and sudden.

[This is illustrated by the following case of Hartshorne's: "I have a young lady now under my care, for non-assimilative indigestion, of whom I received the following account from a mother of more than ordinary intelligence and power of observation. She said that her daughter was fond of reading aloud, and that sometimes in the middle of a sentence the voice was suddenly stopped, and a peculiar stiffness of the whole body would come on and fix the limbs immovably for several minutes. Then it would relax, and the reading would be continued at the very word it stopped at, the patient being quite unconscious that a parenthesis had been snipped out of her sentence, or that anything strange had happened. She grew much better under tonic and restorative treatment, and gradually ceased to have

these singular attacks; but after about a month's interval, as she was one evening engaged in playing a round game of cards, she suddenly went off into a regular epileptic fit, which was followed by sleep, and she did not recover consciousness till the next morning. This fit could be accounted for by certain errors in digestion, and she has had no recurrence of it, or of the catalepsy, though four months have passed over. So I hope it was epilepsy of an intercurrent or curable sort.

"One feels that this must have been a vain hope, and, had the history been subsequently continued for a period of a year or more, it would probably have shown that the case was one of epilepsy, and not of the 'curable sort.' I remember a much-respected lecturer in this metropolis in whom the petit mal of epilepsy assumed this form. He used to be attacked sometimes in the middle of a sentence, with his hand wielded in demonstration before his class. He would remain perfectly still for a minute or so, with mouth open and arm extended, and then resume his sentence just where he had dropped it, quite unconscious that anything had happened. After a time the seizures assumed the more usual and more fatal form. I have seen several cases of epilepsy, especially in children, the first symptoms of which simulated those of catalepsy." (Reynold's "System of Med.," by Hartshorne.)]

The attack may commence by a sudden stoppage of voluntary movement, a rigidity, and the plasticity which is the characteristic of catalepsy may not ensue for several minutes. The length of time for which awkward positions can be maintained has struck most observers as inconsistent with the voluntary powers of a conscious person. This is one of the means of distinguishing feigned catalepsy; for here, when the fatigue period sets in, coarse tremor of the limb begins and the muscles become rigid.

In the truly cataleptic, a weight tied to the arm will cause it to grad-

ually descend without oscillations. The simulator will endeavor to maintain the limb in position in spite of the weight suspended to an extended arm. If it is suddenly let go, it is said that there will be no jerking upward of a cataleptic limb (John Hunter). Some observers say that the electrical excitability varies, but this is doubtful at least.

Bernheim, speaking of hysterical catalepsy, says: "Catalepsy is sometimes *limp*; the raised-up limb falls at the least pressure. Sometimes catalepsy is *firm* without being rigid. The limbs respond to any movement; they straighten or flex as easily as soft wax; one can stretch out certain fingers and flex others; one thigh can be bent, the other straightened. Let the patient be seated, the head drooping on one shoulder; the different parts of the body put into bizarre positions; it will remain fixed like a jointed manikin in the position given. Sometimes catalepsy is *rigid*, accompanied by a true contracture which only suggestion can undo. For example, an arm is raised vertically; it remains thus contracted. If one would lower it, great resistance is shown; if one overcomes this resistance and then lets go the limb, it will return, as though by a spring, to the first vertical position. This is a true rigid catalepsy which may be called tetanic. If, as soon as the patient is asleep, one raises the arms or legs, without speaking, they become immediately rigid, as though tetanized into the given attitude. In some patients the whole body can be thus immobilized in "tetany" so well that one can put the head on one chair, the feet on another, and press upon the body without interrupting the contracture."

The *duration* of a cataleptic attack may be momentary or may last hours or even weeks. In that case there may be intermissions in the catalepsy, which may cease abruptly and return again as suddenly, or may pass away slowly with sighs and a dazed expression as if the waking is from sleep.

The attacks may be grouped close together with long intervals of freedom, as is the case in some epileptics. There may be few or only one in a lifetime. The patient may be quite well between the attacks, or there may be a state of lassitude.

Although consciousness appears to be suspended, it is so only in those cases which are of an epileptic character; for critical examination shows the accessibility of the patient's consciousness, and many patients have related afterward what went on during their attack. Indeed, even when marked catalepsy is present, the eyes may evidently follow what goes on. An example is the case reported by Bondurant (Med. News, 1894), in which catatonic stupor and ensuing dementia occurred after typhoid. Many such incomplete catalepsies are reported by Latron during the course of infections and intoxications. But there are cases where animation is nearly suspended, the patient appearing moribund.

[Of this type 2 were reported by Macdonald. They were cold, rigid, with absent reflexes, pupils dilated, breathing and pulse indistinguishable, and the heart sounds were inaudible. Both recovered.

The case reported by C. S. was less fortunate. It was a child of 8 months who had a temperature of 104°, and who for several days passed periodically into a cataleptic state during one of which she died.]

**DIAGNOSIS.**—**Tetany** cannot be mistaken, on account of its characteristic attitude and spasmodic nature; besides which, disturbances of sensibility and consciousness do not occur.

**Epilepsy** when convulsive is so characteristic that no mistake can be made, but the "absences" of petit mal may show cataleptic phenomena.

**Simulation.**—The suspension of a weight from the arm slowly brings it down when the catalepsy is not feigned, and when the weight is dropped the feigner's arm flies up or becomes rigid. The oscillations which normally occur when uncomfortable attitudes are prolonged will reveal the simulator even although he may successfully resist painful stimuli and appear oblivious to surroundings.

**Death** produces a flaccidity followed by rigor without waxy plasticity of the muscles. The heart will not be heard by the stethoscope; a cold mirror will not be dimmed; but the best test is the ophthalmoscopic picture, for no degree of catalepsy reveals the extreme blanching of the fundus seen after death.

**Narcolepsy**, another syndrome without nosological significance, may or may not be cataleptoid. The distinction is of little importance.

**Tetanus.**—The full consciousness of the patient, the spasmodic nature of the rigidity, and the pain prevent anyone from mistaking this disease for rigid catalepsy.

**Ecstasy.**—The distinctions drawn by Tuke can hardly be held to. Of course, the trance state is usually sought deliberately with a definite objective, while catalepsy appears to be accidental. But there is such a thing as autohypnosis with or without deliberate intention. That the

ecstatic can move in accordance with the ideas which rule him is quite true; but the same is true of some types of catalepsy, more especially in catatonia. The contemplative attitude, too, is quite frequent in catatonia.

**Psychasthenic rumination** might be mistaken for catalepsy. A patient of my own illustrated in a marked degree the resemblance between these two conditions. She would suddenly stop even in the middle of the street, remaining motionless, perhaps in a most awkward position, completely indifferent even to the danger of being run over. There was a rapt look and the breathing became shallow. There was no muscular rigidity or active resistance. But true *flecibilitas cerea* was lacking, and the patient could be aroused from the abstracted state, for there was not the great insensibility to cutaneous stimuli which is found in the cataleptic.

**ETIOLOGY AND PATHOLOGY.**—Neuropathic heredity is by most authors claimed to be frequent in those who suffer from catalepsy. Although commonest at puberty, catalepsy has been reported of a girl 3 years of age (Jacobi, 1885), and in children of 1 and 2 years of age (Strumpel). The condition is apparently commoner in females than in males, in the proportion of 80 to 68, according to Puel.

Predisposing factors are said to be malnutrition and prostration in neurotic individuals. When the pathology is discussed, it will be seen that toxins are the most efficient cause.

The removal of scybalæ caused the catalepsy to disappear in a case reported by Austin. Worms are said to be a cause by Hammond.

Reflex irritation appears to have provoked attacks in some cases. One occurred in a negro boy after inordinate eating of muscadines, of which four quarts were removed from the rectum by enemata, with complete relief of the catalepsy. There were incontinence, fixed pupils widely dilated, and no pulse or respirations (Loftan).

Emotions frequently determine an attack, especially such as occur during a moral shock, a fright, or in religious exhortation. Prolonged apprehension, grief, hatred, jealousy, or the terror provoked by bad treatment are invoked as causes.

Catalepsy has occurred apparently in consequence of intracranial tumor, abscess, hemorrhage, injury, and meningitis. It is quite rare in any of these conditions, but it is not difficult to understand how any of them may interfere with cerebral function in a fashion to inhibit the volitional aptitude required to break a cataleptic attitude.

The cataleptic state is interpreted by many psychopathologists as a consequence of an unrestrained cerebral automatism. This conception makes it easy to understand its frequency in such a congenital defect as idiocy, which is characterized by the failure of development of the structures which permit of the control of the automatic functions by associated experiences.

Case of catalepsy in a boy aged 15 years whose first symptoms were a series of three fits in six weeks. He would first become very stiff for a short time and then jerk himself about, but he had never fallen, as there had always been time to recognize what was about to happen and to get him into a chair. There had

not been any passing of urine in these attacks, neither had he ever bitten his tongue. There was no history of fits of any kind in any other member of the family. The last attack occurred about two weeks before the patient was first seen, and was apparently followed by a state of stupor, in which the boy would not feed himself, and had to be made to pass his urine. Otherwise he had been in a condition of blankness. When first seen by the writer the boy was in an absolutely passive condition. He allowed his limbs to be put into any position and made no attempt either to resist or to alter their attitude. He was, however, alive to painful stimuli, and resented pinpricks by frowning and finally by turning his body away from the stimulus. The only muscles which were active were those of the eyes; these were moved voluntarily, and the patient watched proceedings with interest. The general condition was very good, the boy being well grown, and with remarkably well developed muscles.

Shortly after his admission he would not swallow what was put into his mouth, and nasal feeding had to be instituted. After the first meal given in this way, he took his food perfectly well if it was placed in his mouth. On the eighth day he developed a very slight but definite squint, the left internal rectus apparently being at fault. This, after varying from day to day, disappeared within a week of its appearance. The patient was treated with galvanism and massage, and, although at the time of application he seemed to improve, he remained in the state described for over sixteen weeks. During this time he never, apart from electric stimulation, made a single voluntary movement. He lay on his back staring at the ceiling and generally soaked in urine. While being galvanized he turned himself about in order to evade the battery, and on several occasions shouted out, but as soon as the current was taken off he relapsed into his former state. Some

ten. weeks after his admission contractures of the fingers made their appearance, and any effort to extend them met with the most violent resistance. This was followed by flexion of the legs on the thighs, and of the thighs on the trunk, but the mental condition remained just as it was, and the limbs when straightened could be molded in the same way as when he was first seen. Sixteen weeks after his admission the patient was suddenly heard singing in the night, and shortly after he spoke a few words apart from electric stimulation. From this time he recovered rapidly, but for some time he was unable to feed himself and to speak; his muscles were in their original state of waxy flexibility. Thus after having been given a plate of rice and a spoon he would sit and stare at the food without making the least attempt to eat it. Then when some was lifted into his mouth he would start feeding himself and would continue to raise the spoon to his mouth long after the plate was empty. When told to stop he would obey slowly. If he was questioned, he would at first make no effort to answer, neither would he look at the questioner, but after a long pause he would reply in a peculiar monotonous tone. This transition state passed off rapidly, and the boy assumed what was probably his normal condition. This was one of irritating stupidity, mingled with a low degree of cunning. The temperature through the whole period of his stay in the hospital was normal. There was never any albuminuria. There were no signs of any cerebral trouble, and a diagnosis of hysteria was made. This was confirmed by the appearance of the contractures. A diagnosis discussed was one of postepileptic stupor, but the length of time which had elapsed between the last fit and his admission, fourteen days, put this out of the question. Then, again, the fits were not perfectly typical of epilepsy. Of the many hysterical manifestations the case conformed most

closely to that known as *catalepsy*. Core (Lancet, June 19, 1909).

The direct action of poisons in facilitating the cataleptic state in certain cases is indubitable. It makes no difference whether the poison, like lead, alcohol, or morphine, comes from without; whether it originates from micro-organisms, like the bacillus of typhoid, tubercle, or malaria; or whether it is elaborated by the patient's self, as in disorders of the glands, or during retention of matters which should be eliminated, as in uremia.

An epidemic of icterus in children, associated with catalepsy was reported by O. Damsch and A. Kramer some years ago. The children held their limbs motionless in whatever position the examiner placed them. This condition persisted for about nine days, when it was followed by slow improvement. The liver was enlarged in all cases, but was not tender. The cases all recovered gradually. EDITORS.

It is not credible that edema of the central nervous system is the means through which these poisons act, as was maintained by Traube.

The influence of alcoholism in the genesis of catalepsy has been demonstrated by a number of cases.

[After drinking heavily for some years of rum, absinthe, and wine, a man aged 33, whose father had become insane from drunkenness, was brought to the special police infirmary in Paris, having been arrested for running naked through the streets the night before. He did so because of the belief that his life was being threatened by individuals whom he thought he saw close by. This had occurred after some days of discomfort, during which he had not slept at night and had been confused and agitated.

When he entered the consulting room he was like an automaton, walking slowly and stopping as if transfixed by fear. He stayed in this cataleptic position, his brow



beaded with sweat, his eyes staring fixedly, mute and deaf to all solicitations and unresponsive to pain. The skin was warm and the pulse frequent and bounding. Although the muscles seemed to shake, his limbs retained any position which they were given just as in catalepsy. He stayed in this state five hours, but was not unconscious, for when asked if he saw wild animals he made a slight inclination of the head. He passed out of this attitude suddenly, screaming that there were fifty men pursuing him to kill him. After two hours of this he had another short cataleptic phase, upon which supervened a delirium of a less wild character. (Garnier, *La Folie à Paris*, 1890.)

A tall, strong, married woman aged 40, with slight edema of the legs and congestion of the face due to a mitral incompetence, had latterly become irritable and negligent on account of her alcoholic habits. Suddenly one night began nocturnal delirium. A few nights later this became transformed into a violent and typical maniacal delirium with terror, in which, however, psychomotor hallucinations played a large part.

When admitted to the asylum she rapidly fell into a stuporose state, in which she fell to the floor. Then began the catalepsy, the description of which I translate from Toulouse, the observer:—

"When seated she is immobile as a statue, arms hanging along the body, head straight, eyes looking down. When approached, spoken to, and shaken, there is no reaction. Although the eyes are open, the eyelids too are motionless, and yet no tears fall over the cheek. She breathes superficially twenty-three times a minute; the pulse is 88 and irregular in volume. The knee reflexes are exaggerated; there is hardly any reaction to a pinprick; the arms fall only very slowly when lifted up. The pupil is absolutely immobile to all forms of excitation, including strong odors and metal heated to 140° F., and yet sight is present; for the patient recoils when a finger approaches close to the eye. No stimuli alter the rhythm of the pulse and respiration."

That evening the patient slowly came out of this state, during which she remembered all that had occurred. The

sensations she declared had been blunted, and although she was frightened she was unable to move.

A month later, when she was discharged, the pupil contracted readily to light, but it was only slightly modifiable by sensory stimuli.]

*Cannabis indica* was the intoxicant which produced cataleptic phenomena in a case reported by Coudace in 1859. Insensibility was complete; the reflexes were abolished except those of the pupils. There was trismus and total catalepsy, which was maintained for three days. A state of stupor lasted five days, and he had no memory for what happened during his attack.

Absinthe was the cause in a case reported by Draper.

In the preceding observations the catalepsy was complete, which corresponds to the pervasion of the toxin throughout the system. In each case the catalepsy disappeared concurrently with the cessation of the intoxication which provoked it. It is hard to say, in the alcoholic cases, whether the cataleptic susceptibility of the patients was due to their absorption; by the terrifying hallucinations of their delirium, or whether it was due to the dulling of their perceptive faculties and the absence of the feeling of fatigue.

Toulouse's case, as in one poisoned by hashish, might be explained in the latter way because of the absence of reflexes and the paralysis of the pupil. But in the first case the psychological explanation cannot be excluded.

Although rarely reported, catalepsy in typhoid fever must be much commoner than supposed; for it might easily escape notice unless sought for, as it is rarely of the complete type. Bernheim found it very often, some-

times of the flaccid type, but more often elastic or rigid, although the arms will usually remain as placed, and when pushed quickly stop motionless again. In some cases a rotatory automatism can be provoked, as in hypnotized subjects. Some of the patients fall into spontaneous hypnosis. He explained the condition as being due to an adynamic psychic state caused by intoxication of the disease, which diminished intellectual initiative. It is a state which is perhaps normal in certain individuals, the hypersuggestible.

[Three such cases are described by Dufour. The first of these was completely cataleptic, but the stupor was not marked, consciousness being retained throughout the course of the disease. The attitudes responded to verbal command, her suggestibility being extreme. Like an automaton, she laughed when told to do so, and even tears would come on request. The phenomena ceased as defervescence began. The family history was defective. In another case which died the stupor was intense.]

Catalepsy in intermittent fever was reported by Dionis as long ago as 1709, and again by Bourdin in 1840 and Boerhaave in 1753.

Catalepsy has been observed in tuberculosis, though rarely.

Cataleptic symptoms were observed by Epstein (*Revue men. des mal. de l'enfance*, Jan., 1897) in 8 rachitics aged from 18 months to 3½ years. The phenomena were manifested by the persistence of the position given to a limb. When the leg was raised, for instance, it was maintained in this position for a long time, in one case even as long as forty minutes, and then falling very slowly. If the position of the limb or parts of it was changed, even to a very uncomfort-

able attitude, the immobility would be maintained for an equal period of time. This phenomenon was more constant and distinct in the leg than in the arm. There was no tremor in the limb. During the cataleptic state the reflex excitability seemed diminished.

**PATHOGENESIS.**—The variability of the psychological symptoms arising in toxic encephalopathies does not depend upon differences in the quality of the poison or in its distribution in different parts of the cerebrum so much as it does upon the differing disposition of different people.

It must be borne in mind that catalepsy is due only to the interference with the normal potentiality of associating together the impressions of sensation with the memory we have of former sensations and their associations. This interference may be due to gross lesions, as in a case where small rarefactions were found in the midbrain. Any cause so gross as this, however, is rare.

But that there are lesions in some cases caused by toxins is rendered likely from the researches of Donetti (1897) upon experimental uremia. He declares: "The method of Golgi has shown the presence of cells with prolongations showing atrophic varicosities. Along these prolongations are numerous little round bodies irregularly distributed, which when powerfully magnified look spongy, and appear almost attached by a short stem to the cellular prolongations. The prolongations show also numerous irregular fractures. These lesions are more marked in the cortex, and rather less in the cerebellum and in the spinal cord, where here

and there one can find cells with normal prolongations. Some cells show disintegration of their body, but upon the value of this I cannot give an opinion.

"The prolongations of the cells of the neuroglia show alterations similar to those mentioned above, and one can easily distinguish, among the numerous prolongations, swellings and contractions.

"Nissl's method has not revealed any important lesions in the cortex; on the contrary, it has shown considerable modifications of the structure of the large cells of the spinal cord and the cerebellum.

"The alterations are concerned, first, with the place and volume of the nucleus, which is slightly vacuolated, and which one finds more than normally placed at the periphery; secondly, the distribution of the chromatin substance, which in many cells is reduced in quantity and modified in appearance. One finds in different points of the cells clear, unequal zones, which give a vacuolated appearance; the remaining chromatic substance is finely broken up. In many of the cells in which there are no vacuoles, one always finds the chromatic substance finely granulated. The prolongations are difficult to color on account of the loss of chromatin; there is nothing unusual in the achromatic substance." (*Thèse de Paris, 1900-1901.*)

We cannot, of course, be certain that lesions of this kind, even if they occur in human beings, are the actual cause of uremic catalepsy; for it is not unlikely that the poison itself which appears to be the cause of them is the real agent which provokes cataleptic phenomena directly. In view of the

fact, however, that alcohol is not only toxic in the sense that it interferes with the proper function of nerve cells and fibers, but is capable of producing actual changes therein, we are far from a decision of the question whether histological changes must not be incriminated in the pathogenesis of toxic encephalopathies, as they undoubtedly are in the case of such a toxic neuropathy as multiple neuritis.

Very small doses of poison seem to have sufficed for an attack in some cases. Thus, nine-tenths of a grain of hypochlorite of morphine produced an alternation of catalepsy with trismus, opisthotonus, and convulsions in a man reported by Eulenberg. Morphine was surely the direct cause in Meig's case, for there was profound stupor and the usual symptoms of opium poisoning along with the catalepsy, from which the patient recovered after purges, enemata, and bleedings. He quotes a case of some weeks' duration from Darwin, said to have resulted from mercurial poisoning.

Lead as a cause of catalepsy was urged by Tanquerel des Planches. From his description, which follows, it is not at all certain that his cases were not in reality due to a nephritis, for he makes no mention of the examination of the urine or of the necropsy.

["The patient appears to be calmly sleeping with the eyes closed. When pinched, pulled, or the skin burnt anywhere, the patient gives no sign of feeling. It is impossible to awaken or to fix his attention. If the hands, forearm, the arms, legs, or thighs are placed in any position, the most tiring or the most comfortable, they remain thus for several seconds or even for two or three minutes, then they waver a little and finally drop onto the bed. If the trunk is stiff, the pa-

tient cannot be made to sit up. When the trunk is supple, the cataleptic, put in a sitting position, remains like a statue for several hours, then falls back.

"When this condition has lasted a quarter of an hour or several hours, as the case may be, the scene changes completely: the patient, with eyes closed, begins to make very expressive movements with the limbs, the head, the face, and the body. These are co-ordinate movements, and seem all to be the expression of the same idea. But from one minute to another the expression of the mimic changes. Sometimes the patient is silent; sometimes he calls aloud, makes efforts to speak without succeeding; his language is only unintelligible mutterings. If pinched at this time he makes quick movements of defense, showing he feels keenly. The arms can no longer be placed in a fixed position. They resist the position that one would give them. When these movements and cries have lasted several minutes, perfect calm is restored and the patient falls again into a cataleptic state; then the mimicking movements return, succeeded by cataleptic coma—and so on.

"Momentary intelligence seems still to be present. Thus, we have seen a patient show by significant gestures that he wished to drink, then all at once throw the fluid which he was holding in his mouth on to someone. Then the cataleptic state returns again with complete insensibility and conservation of the limbs in given positions.

"After several hours or days of these changes from lethargy to agitation the patient's eyes open suddenly, and he asks to eat or drink, etc. If one questions and stimulates him, he talks with ease. Left alone, he speaks often to himself, expressing with great volubility an infinity of incoherent ideas. In the middle of this disorder of thought, if one quickly succeeds in fixing his attention, he will answer a word or two quite correctly; then he continues his wanderings. The same idea is the subject of his delirious thoughts during several minutes; then it changes. Sometimes the patient is greatly agitated: he tries to raise himself; he exhorts, abuses, tries to fight and bite, etc., anyone who approaches him.

"The following day the delirium gradually disappears, or presents the exacerbations and remissions of which we have already spoken. Quiet delirium alternates with raging delirium and somnambulism." (*Traité des maladies de plomb.*)]

During narcosis by ether or chloroform cataleptic phenomena are very common, but they usually disappear as narcosis deepens and as the drug is excreted. Afonski in 1885 reported a case which followed chloroform.

Many cases are reported during alcoholic insanity in individuals of neuropathic type.

Disorders of the internal secretions seem capable of producing catalepsy. Extirpation of the thyro-parathyroid organ in dogs was shown by Blum and Pineles after Lundborg to cause catalepsy. Parhon, of Bucharest, confirmed this (1908). The relationship of the phenomena to those of tetany may have significance.

Muratoff described (1907) pathological changes in the thyroid gland of patients with catatonia. He declares that those with catatonic stupor showed atrophy, and those with catatonic excitement showed a hypertrophy of the thyroid tissue. Opothrapy, however, had no effect upon the symptoms, while in catalepsy John Rogers (*Amer. Jour. of Insanity*, July, 1896) found thyroid treatment efficacious in 2 cases in which all other measures had failed.

Berkley has had a limited success in the amelioration of cases of dementia præcox by operation on the thyro-parathyroid organ.

**CATALEPSY IN HYSTERIA AND HYPNOSIS.**—The induction of catalepsy in hypnosis is one of the classical features in all the descriptions. Since the work of Babinski, it is clear that both hypnosis and hysteria are

phenomena induced by suggestion and do not differ in essence. That in the latter catalepsy is clearly induced and in the former appears to be spontaneous is only a superficial view; for, since the memorable discussion on hysteria at the Neurological Society in Paris, 1907 (N. Y. Med. Jour., Jan., 1909), it is clear that the phenomena of hysteria itself are induced, and it only requires some little pains by psychoanalysis to discover their source in individual cases.

The catalepsy of hypnosis is described as follows by Bernheim: "I will take a patient in the hypnotic state, whether apparently asleep or not. I will show upon him the effect of different suggestions. Let us begin with the easiest, motility. And, first of all, catalepsy. I raise the arm, it falls down. In others the arm will remain raised. In this case it is enough to leave it several seconds in the air for it to remain stationary in the given position. In some cases an explicit order must be given for the patient to realize what is required to assume the positions of cataleptic character. The same attitudes can be given to the legs, but not for long. This cataleptic state does not last indefinitely. In fifteen or twenty minutes the limbs become fatigued and fall gradually or rapidly, the legs more quickly than the arms.

"Catalepsy cannot be produced in the same way or with the same facility in all. Here is a case which is only slightly influenced; the raised limb remained as though the patient had forgotten to lower it. But if I say, 'You cannot lower it; try to do it,' he makes an effort to recover himself; the challenge I have given him awakens his intellectual initia-

tive, and he lowers the limb. However, if I begin the experiment again without appealing to his initiative, the cataleptic attitude is once more assumed.

"Here, on the contrary, is a subject more strongly influenced. I challenge him to change the position of his arm. I ask him to try with all his power. He tries; but in spite of all his efforts, he cannot displace it. This patient changes it only very little, beyond which he cannot go. Between the catalepsy which the patient can interrupt and the catalepsy which is completely irresistible, one can observe all degrees, and these degrees are, in my eyes, one of the best ways of judging the power of the suggestive influence, in appreciating just at what point the will is paralyzed or powerless."

The likeness to hysterical catalepsy is well shown in the cases described below:—

[Case of frank catalepsy in a young girl who lived in an apartment house. In the flat above the one in which she lived a musician played frequently on the piano. For some time she paid no attention to the music, until one day it annoyed her; this annoyance resulted in a major attack of hysteria. After this the hearing of music would always produce an attack. These convulsions were followed by profound sleep, during which she was indifferent to all peripheral excitations, and the muscles remained in a state of waxy flexibility. (Bérillon.)

*La Dormeuse de San Remo* is similar to the case given above, in that her attacks were definitely provoked by an annoyance, which in her case consisted of a rebuke. She had been in the habit of wandering away at will in a dreamy state, and would sometimes, during these divagations, fall into catalepsy. In the attacks which were observed she showed œsophagismus, pharyngeal anesthesia, cutaneous insensibility in various zones of the body,

with very marked catalepsy. After this series of symptoms she would awaken quite slowly, and loud sounds would cause her acute pain. While in these deep sleeps, she appeared to be inaccessible to suggestions or any external stimuli whatever. (Farez.)

The following case, which was adjudged insane and kept in an asylum for some years, showed remarkable psychogenic factors, in that her attacks appear to have been due to frights she received in childhood. The author called it, however, dynamic catalepsy. I abstract from his description:—

"The patient was coherent and intelligent, also excited and distressed. Her expression was anxious, the teeth clenched; the lips were parted and the jaws locked; the masseter muscles were contracted into hard knots. This condition followed a blow on the cheek given by her husband. While answering questions by nods and shakes of the head, she suddenly slipped from her chair to the floor, showing tetanic and clonic spasms, partial, complete, symmetrical, and irregular by turns. First opisthotonos, then thrown forward, then twisted round, then writhing like an eel. Slow undulations of spasm passed over her from head to foot, producing movements of limbs, like a dog dying of hydrocyanic acid. The tonic spasms suddenly became clonic. Her face was in turns contorted into the expression of rage, fear, sneering; fixed, rigid stare; eyes rolled, and the corner of the mouth was drawn down onto the chin; the skin of the neck was rigid. Then there was rigid tonic condition of whole muscular system. The muscles were as hard as boards; the movements were slow and of great force, 'influenced by diseased will' (*sic*). During the spastic movements there was complete insensibility to surrounding objects. When the fits ceased the intellect recovered quickly and the patient talked freely and collectedly.

"She was an hysterical, excitable person, and had had fits from fright since the age of 10, which continued twice a week until marriage at 15; they were not so frequent after that. The grandfather and paternal uncle had fits. Eight of her 9 children died, 7 in convulsions."

**CATALEPSY IN RELATION TO PSYCHOPATHOLOGY.**—In none of the above cases was the psychological mechanism unmasked. The authors, indeed, do not appear to have suspected that the mode of genesis of their cases could have been discovered through proper psychoanalysis, nor did they clearly see the therapeutic import of an hysterical pathogenesis. They seem to have had glimmerings of the rôle of suggestion in their somewhat crude attempts at hypnosis. The means they adopted to arouse patients from their catalepsy were weak and ineffective. Empirical though it was, the method used by Raffegeau proved a successful exception. His case was that of a girl of 13 years, who had been four months in a lethargy, during which she kept her mouth open in the day and closed it at night. All attempts to wake her failed until, in an attempt to diminish the volume of her hypertrophied tonsils, Raffegeau applied the thermocautery. The second time after this was done she arose from her long sleep definitely.

Attempts to analyze the feelings and ideas during catalepsy began with Janet's studies of hysteria. His researches led him to believe in the rôle of subconscious fixed ideas as perturbers of thought which interfered with the will, sometimes to the extent of creating complete immobility. Such ideas or feelings were usually of a painful nature and the patient tried to evade them. It was then when they gained the ascendancy that they developed the peculiar behavior which led the patients to the Salpêtrière, where they were studied.

In recent years psychopathology has received much more wide atten-

tion, and nowadays numerous analyses are being made. But as catalepsy is only one of the numerous ways in which disordered functions of the mind are revealed by the same patient at the same time, it must be studied in conjunction with the other phenomena. This would lead us far beyond the bounds of this article. Moreover, the matter will be taken up in its broad relations in the course of the articles on Hysteria, Psychopathology, and Psychasthenia, in the elucidation of which methods of analysis play a large part.

**ECSTASY.**—Certain states of trance are closely allied psychologically to that of hysterical catalepsy. In trance or ecstasy the subject remains for a long time, as it were, glued to the same position with the eyes fixed, indifferent to extraneous stimuli. Indeed, abstraction may be so complete that the patient is insensible to solicitations from without, and the limbs when handled by another person will remain as they are left, just as in catalepsy.

The cataleptic state has played an important rôle in the history of religions. A discussion of its contribution to the doctrine of the nature of the soul and its power of leaving and re-entering the body (animism) would lead us too far. Nor can we pause to discuss its significance in the sacerdotalism of oracles and holy shrines. Even in history, catalepsy has played a part, Joan of Arc having exhibited the trances of which cataleptic attitudes are a part.

The origin of the trance is well known to be the fixed contemplation of some image or idea to the exclusion, as far as possible, of other mental content.

[This is hardly the place for a full description of the phenomena of trance. The reader is referred to "*Le Chateau Intérieur*" of St. Theresa and "*Le Moyen de faire Oraison*" of Madame Guyon. These wonderful dissections of the human soul portray the trance state most convincingly.

But similar cases have been studied by modern psychopathologists. Thus, one of Janet's patients declares: "I have felt an ineffable sweetness on my lips; soon they become glued together; the limbs become numb, but this numbness is full of sweetness. A voluptuousness spreads over all, and I feel as though I were swimming in an atmosphere of delight." Then, in the state of complex ecstasy, "I have seen," she says, "the holy sacrament in a light, a sudden gleam, a flash as one never sees it, that completely fills me with inexpressible feelings. An internal voice makes me understand that by the communion I carried Jesus with me and I was like unto a living remonstrance."

In this patient, there was a permanent attitude of contracture in portrayal of the crucifixion, along with cataleptoid phenomena.]

States similar to the trance sometimes begin suddenly, quite apart from deliberate intention of the patient to provoke them.

[Janet's classical case, Marcelle (*Névrose et idées fixes*), is a striking example: "All of a sudden, without appreciable warning, she stopped speaking and remained quite motionless, the face transfixed. She seemed no longer to hear me, did not react when pinched, kept the eyes wide open without moving, and finally left her limbs for some time in the air in the position I gave them. This kind of an attack did not last more than a quarter of an hour. She came to with sighs, tears in the eyes. Then with an effort she began to speak as if nothing had happened. When interrogated she replied, 'It is nothing; these are my ideas; they have gone; it is like a cloud which passes.'"

The ideas which caused this state were discovered by Janet by methods of distraction such as automatic writing and hypnosis, as well as by direct questioning

during and just after the fit. The ideas were vivid enough to resemble hallucinations, although the patient did not hear voices, but felt that someone spoke to her. She dwelt on the belief that her family and everyone detested her, that she should in consequence die, and ought not to eat, speak, or move. They were really souvenirs of certain resolutions which in the past had the motive of a love disappointment long since recovered from.

The cataleptic state was the result then of, so to speak, the orders given her by the voices of her trance or dream. The rôle of the thoughts of a dream in determining behavior after the dream has ceased is quite important in the causation of delusional states with erratic conduct. Hence, the catalepsy which so arises may be either the expression of belief of the subject in his impotence in consequence of the fantastic ideas of his dream, or it may be merely the fixity of attitude due to the extreme abstraction from external influences due to concentration upon the ideas of the trance.

That the patient is not really inaccessible to stimuli is shown by kymographic records made during the trance. (Janet, *loc. cit.*)]

**TREATMENT.**—As catalepsy is merely a symptom, it will be highly irrational to direct treatment exclusively to it. When epilepsy is the cause, the treatment must be directed to this disease. When intoxication or infection is the source, it is the treatment of this that should occupy the physician's attention. After the removal of the cause, the catalepsy will disappear of itself.

But when hysteria is in question, catalepsy may be the sole manifest symptom. In that case it is the morbid sleep which must be successfully counteracted before one can undertake the radical removal of the hysterical tendency by analysis and re-education.

*Arousal from cataleptic sleep* should be no harder to effect than the re-

moval of artificially induced hypnosis, provided that the physician understands the nature and mechanism of hysteria and is resourceful and determined in gaining access to the patient's attention. It is in such a case that isolation from friends is of particular value. When this is accomplished, powerful sensory stimuli may be used if an affectation of studious neglect fails to impress.

Once a response is obtained, the treatment becomes that of hysteria in general (*q.v.*).

[According to the late Prof. J. T. Eskridge, the treatment of catalepsy should first consist in measures for the relief of the paroxysm and the employment between the attacks of those agents most likely to aid in toning up the nervous system, together with such changes in the daily life and surroundings of the patient as are best adapted to improve the mental state.

During the paroxysm it is always well to unload the bowel with a **high enema**, consisting of about 3 pints to 2 quarts (1500 to 2000 c.c.) of warm water to which 1 or 2 ounces (30 or 60 c.c.) of the tincture of **asafetida** have been added. After the bowels have been thoroughly opened in the manner indicated,  $\frac{1}{2}$  ounce (15 c.c.) of the tincture of asafetida in about 4 ounces (120 c.c.) of water may be thrown into the bowel high up and allowed to remain. If the attack is severe 15 or 20 grains (1 to 1.3 Gm.) of **chloral hydrate** may be added to the tincture of asafetida for the small enema, in which case milk should be used instead of water. If the stomach contains any undigested food  $\frac{1}{10}$  grain (0.004 Gm.) of **apomorphine** may be given hypodermically. A free



emesis even when there is no undigested food in the stomach may aid in aborting the paroxysm.

To shorten the attack inhalations of **amyl nitrite** or an hypodermic of  $\frac{1}{100}$  grain (0.0006 Gm.) of **nitroglycerin** may be employed with advantage. Cool applications to the head and passing a piece of **ice** up and down the spine several times and following this by briskly **rubbing** the spine with a coarse towel greatly aid in establishing reaction. A **mustard plaster** to the nape of the neck and one over the stomach have the same effect. Diffusible stimulants, especially **ammonia**, may be used with advantage. **Ether** or **atropine** hypodermically is also very useful.

During the intervals the treatment and general management are of considerable importance, and should receive as much attention as in a case of hysteria. In the first place careful attention should be paid to the food and organs of digestion. The **diet** should be nutritious, easily digested, and abundant. If necessary, digestion may be aided by the ordinary means. A free action of the bowels should be obtained each day. **Iron**, **arsenic**, **quinine**, and **strychnine** should be employed in the building-up process.

Systematic, but not violent or overfatiguing, **exercise** should be insisted upon for all those who are not too weak. A little **gymnasium** can be arranged in most bedrooms, and the beneficial results to be derived from regular exercise for a few minutes night and morning can scarcely be estimated until after one has tried it. A cool or **cold sponge** or **plunge bath** should be indulged in night and morning, following the exercise. At

the same time the patient should be kept in the open air as much as possible.

If the patient is a child or young adult the education should be judiciously supervised, and all oversentimental and emotional books excluded. Companionship for such patients, be they children or adults, is of great importance. In short, everything in reason that tends to **develop** muscle and improve the **mental and physical condition** of the patient should be encouraged, while exhaustion, depressing agents, poor nutrition, and emotional excitement should be avoided if possible.

Rogers obtained beneficial effects from **thyroid-gland** medication after all other measures had failed. Ed.]

## CATATONIA.

### THE CATATONIC STATE (MELANCHOLIA ATTONITA).—

The cataleptoid attitudes of insane patients have been recognized from the first. They were, however, not clearly grouped together until the famous study of Kahlbaum in 1874. The condition he so clearly described he called "catatonia."

**SYMPTOMATOLOGY.**—The condition is constituted by the three characters known as negativism, automatic suggestibility, and stereotypy of attitudes and movements. Besides these there are always such symptoms as peculiarities of character, diminution of attention, loss of power to work, and an apparent emotional indifference, with loss of will power and intellectual activity accompanied by the fixation of the somewhat restricted field of ideas of the intelligence which remains. As a result of this limitation of the intelligence delusions

show themselves, usually incoherent in appearance, but often shown by psychoanalysis to cohere to a state of feeling which is masked at first by the negativism of the patient. The variability of the symptoms is characteristic, and the alternation of agitation with stupor is the rule. Either of these may preponderate over the other during the whole course of the disease.

Little as agitation may seem to conform to the idea of catalepsy, careful observation shows how stereotyped are the movements, expression and words, and even the absurd acts of the agitated catatonic patient. Even the fugues (ambulatory automatism) and homicidal attacks of such patients show marks of stereotyped automatic activities.

Of the more demential and delusional symptoms further notice will be taken in the article on dementia præcox (*q.v.*); but of the three cardinal symptoms—negativism, automatic suggestibility, and stereotypy—more must now be said.

(a) *Negativism* was defined by Kahlbaum as “a constant and instinctive tendency to resist all urging coming from without.” This tendency—a madness of opposition, as it was formerly called—is shown in the resistance of the patient, not only regarding the movements of the limbs, but also to all entreaties or orders. He refuses to speak, to write, to get up, to walk, to eat, to go to bed, to dress himself, etc. The refusal to talk is known as mutism and is quite a frequent symptom; it may last for days, in some cases for years. The negativism may reach the degree of retention of urine, feces, and saliva, with most unpleasant and sometimes

dangerous results. Absolute refusal to eat is also a common result.

This mute resistance to solicitations from within and without may be transcended into a manifestation of contrariety consisting of performance of the opposite of the act requested, just as in a capricious child. Weygandt called this “active negativism.” For instance, a patient asked to open the mouth would close it; when asked to look at the physician, would turn away the head, and so forth. The symptom is accounted for by the psychological law that most conceptions are associated with their contradictions. For instance, it is hardly possible to conceive of darkness without contrasting it with the idea of light, of heat without the contrast of cold. Even sensations without essential connection are habitually contrasted; for instance, sweet with sour. The same law holds for more complex recollections. Séglas has supposed that negativism is caused by a comparative preponderance of the contrasting idea, accounted for by the dementing process, which interferes with the clear elaboration of the idea which should be properly aroused by the stimulus to which the negativism is the response. So that negativism is not necessarily delusional at all, but merely the dissociation of primitive intellectual elements which control the movements of higher mammals. It is a dysboulia (disorder of will) if one conceives the will merely as the power of the organism to react efficiently toward attainment of desires.

This feature distinguishes the negativism of dementia præcox from the obstinacy of melancholics; for al-

though timidity and constraint before others may be present unsuspected by the examiner in the negativistic manifestations of dement, yet the negative reaction frequently passes away in a few moments when the normal volitional response comes to the surface, and the patient's response is silly, purposeless, and not invariable; whereas in stuporous melancholia the negativism is due to the delusions of the patient, and is deliberately adopted and carried out teleologically in strict logical conformity with the false belief of a person in full possession of the will.

(b) *Suggestibility*.—When a conception leading to an act does not arouse in consciousness its appropriate contrast or alternative, auto-critical inhibition cannot be made, the act is performed, and the symptom of "command automatism" is constituted. This ductibility applies not only to spoken words, but to the motor reaction to all sensory impressions. Its result is catalepsy in its most typical state. When carried to its extreme, an ape-like imitation characterizes the patient. They copy attitudes and acts (echomimia, echopraxia) and repeat like a parrot what they hear (echolalia).

The alternation and admixture of negativism with suggestibility is frequent, and so should not lead to clinical confusion.

(c) *Stereotypy*.—This term is used to denote the condition where the absurd attitudes, gestures, or words resulting from morbid suggestibility and negativism are long maintained or often repeated. The patient may remain for days immobile in bed, crouching like a pointer dog, or may bury himself under the coverings, or

he may stand or kneel motionless or double up on the floor, or sit inert on the edge of the bed. He may even stand on one foot for hours at a time. These mannerisms, as they are sometimes called, nearly always show themselves, too, in the face by the fixation of a certain expression, or sometimes even of a different expression on each side of the face (paramimia).

Besides these stereotypies of attitude, we find stereotypies of gesture; these occur as grimaces and facial tics. A very common one is what the Germans call "snautzkrampf," which consists of the puffing out of the cheeks with protrusion of the lips to resemble a pig. The patients will show idiosyncrasy when they shake hands, eat, stand up, or clothe themselves. All their acts are out of harmony with the end sought, and bear the print of automatism.

In speech, this is particularly noticeable. To the theatricalness and exaggerated emphasis of language often shown in catatonia the name "verbigeration" has been given. The peculiar gestures find their verbal counterpart in the coining of new words (neologism), and the mannerisms show themselves in speech by peculiar ways of sounding or deforming certain words.

To the frequent repetition of any of these manifestations by the same patient the name "perseveration" has been given. In some respects this symptom resembles the disorders of movement and language occurring in lesions of the cerebrum known as apraxia and jargon aphasia.

The impulses of these patients are often dangerous, and cannot be foreseen because of their sudden onset

and because of the negativism, which prevents an adequate analysis of the patient's mental state. So much is this the case that the fact that the patient is really a catatonic may be impossible to recognize even by skilled observers. In that case, recourse must be had to the history of the onset and to observation of the physical symptoms and signs, which are more conspicuous than in the other forms of dementia præcox.

Catatonia is a transitional state of insanity passing from melancholia to mania, and thence to complete mental and physical decay. In two personal cases the condition followed an infectious disease; in both there existed modifications in the state of muscular tonicity. In the first the state of contraction was interrupted by periods of arrest, such as tics and trembling of the muscles; in the second the muscular stiffness was permanent. In the first case voluntary acts were accompanied by movements of arrest and change of direction; in the second the movements of arrest, acts of opposition, and resistance predominated, and manifested themselves more when an attempt was made to prevent them. Catatonic symptoms are met with particularly in primary dementia, and especially in the hallucinatory forms of that disease. The motor symptoms are not exclusively seen in primary dementia, and, besides, cases of primary dementia have been reported without catatonia. Nevertheless, it cannot be denied that it is in this form of insanity especially that the maximum of frequency and intensity of these symptoms is seen. They are met with also in hysterical patients, in epileptic demented, in some general paralytics in the second and third period of the disease, less often in senile demented, but with extraordinary frequency in idiots. In this last class of cases there are swaying movements of the body, jumping, clapping of the hands, di-

verse movements of the fingers, contractions of the face, muscular stiffness, etc. These tics, grimaces, movements, etc., do not possess any real significance, but they all have a demential character, and there is an absolute identity of these motor symptoms with the automatic movements of the idiot. The impulsions, the tics, etc., are expressions of cerebral automatism, and are met with not only in primary dementia, but in other mental diseases, as well as in epilepsy and intoxication from drink. All these symptoms have this common condition: there is an absence of direction and of control of the intelligence—they are acts of pure automatism, and, as such, are met with in all states where the intelligence is dulled, where conscience is annihilated—in other words, in most states of mental stupor. Paul Masoin (*Jour. de neurologie*, Feb. 19, 1902).

Catatonia may appear in children, especially during the years from 12 to 15, and does not differ substantially from the adult form. It is often based on a congenital mental defect, and develops from this without being materially affected by outside influences. Many so-called imbeciles with catatonic symptoms have possibly suffered from an attack of catatonia in childhood, and their mental condition may to a great extent result from this. The existence of imbecility has no marked influence on the form and on the prognosis of catatonia. Ræke (*Arch. f. Psych. u. Nervenkrankh.*, Bd. xlv, H. 1, 1911).

**PSYCHOPATHOLOGY.**—Although catatonia is a psychical syndrome (though not of psychic origin) showing a succession of phases of depression, excitement, and stupor with active not strongly systematized delusions and intellectual enfeeblement, the characteristic feature, however, is the peculiar cataleptoid attitudes known as stereotypies and the extraordinary alternations of extreme

suggestibility and strong negativism. These three conditions have really the same mechanism; for stereotypies both of attitude and movement depend upon a perversion of the will through a dissociation of the elements which determine the motor impulses. One of Régis's patients who recovered declared that, however much he wished to speak or to perform an act, he felt himself utterly unable to initiate the movement necessary. On the other hand, a stimulus from without will in some cases cause a response with the greatest facility, producing an extreme docility, on account of which patients will copy the movements of people around them (echomimia, echopraxia), or repeat their words (echolalia), or obey a written or spoken instruction, and go on repeating the act like a machine until they are stopped by further orders, the self-control being so much in abeyance.

Negativism, although opposite in result, is in reality also due to the abeyance of normal self-control. It must be remembered that normal experience has led to numerous associations of ideas in virtue of which every incitation to action calls up the possibility of inhibition of the act, and that every idea brings into consciousness also a notion which is contrary to it. It is only in virtue of this property that the human mind attains the power of judgment.

When there is an interference with the cerebral processes in virtue of which ideas and ordered acts are possible, a dystaxia occurs. In some instances this leads to loss of the power of spontaneous arrest when a tendency is put into play. We have then hypersuggestibility. The start-

ing stimulus may arise from without (heterosuggestion), or from within from a movement, sensation, or idea of the patient's own (autosuggestibility). Thus may arise either repetition of a movement or fixity into an attitude. It is when the intrapsychic ataxia reaches such a degree as to interfere with the assimilation of interfering ideas that negativism results. Then the patient is obstinate in maintaining his mutism, attitude, or movement, because he is like a machine set going or stopped, to which no one has the lever with which to stop or start.

That negativistic attitudes are not maintained indefinitely is due to the oscillations in cerebral conditions which permit of them. These can be influenced to a certain degree psychologically. Thus, annoyance, shyness, or anger, as well as exhortations, may produce changes in the attitudes of catatonics on some occasions.

When patients do just the opposite of what they are asked, like capricious children, it is not from lack of suggestibility, but because the intrapsychic ataxia leads to a predominance of and exaggeration of the idea contrary to that suggested. The defense reaction is excessive.

Results of a study of 12 cases of catatonia. Clinically these cases correspond to the classical descriptions of Kahlbaum and Kraepelin. Catatonia is an acute toxic disease with a definite onset and course, in which the symptoms vary according to the resistive power of the patient, but in which the following diagnostic symptoms are never absent: A prodromal period of gradual onset which leads into the period of acute onset with oral hallucinations, mental confusion, paroxysms of excitement, impulsive action, catatonic spasm of the muscles, a hyperleucocytosis which at

the termination of the acute stage indicates a virulent toxemia. Bruce and Peebles (Jour. of Mental Sci., Oct., 1903).

In a case of late catatonia the writers found focal unilateral cerebellar disease of long standing, apparently quiescent, and beyond question due in large measure to arterial thrombosis. There were no histological nor clinical evidences of syphilis, and the pericardial fluid post-mortem gave a negative Wassermann. Taft and Morse (Jour. of Nerv. and Mental Dis., Sept., 1914).

**PATHOGENESIS.**—Most of the literature on catatonia has a German source, most other writers having refused to acknowledge the autonomy of this syndrome. In recent years the Germans, too, led by Kraepelin, place the disease among the forms of a larger group of a psychosis usually dementing, which in the main is an enlargement of the group formerly described as "adolescent insanity," which also comprises hebephrenia and many of the acute manias and stuporous melancholias of the older writers. To it fail to be added many of the delusional states, some of which were not so long ago classified as paranoia. These, under the title dementia paranoides, have been included, along with catatonia and hebephrenia and simple early dementia, in the group known nowadays as dementia præcox. Most of the German writers separate this from the amentia of Meynert and the Italians. But as it is not possible during the initial attack to determine whether a "*stupide*" phase will be completely recovered from or lead to a dementing psychosis, many French writers, led by Régis, prefer to group these conditions under the rubric of "confusion mentale," of which so full

a description was given in the monograph of Chaslin in 1891.

Régis believes that the catatonic state is due to toxicosis; that in proportion as the intoxication is abundant and rapidly acting, prolonged or of short duration, or perhaps differing with the quality of the toxin, or whether the patient is susceptible, the manifestations may be slight or intense, acute or chronic, show inhibition of psychomotor activity or disorder thereof, give rise to hallucinations or not, deprive the patient of insight and induce delusions or leave him in full consciousness of the abnormality of his reactions.

Otherwise stated, he believes, with Kraepelin, Jung, Stransky, and their followers, in the toxic origin of the dementia præcox group, a chronic disease of which the etiology is obscure, but he disagrees with them for separating the disorder from the more acute toxi-infectious syndromes the etiology of which is clear.

His argument is based upon the similarity of both the physical and mental symptoms shown both in toxi-infectious cases of confusion which recover completely, and those occurring in cases of confusion with stupor and delirium which afterward become demented. Common to both are such symptoms as leucocytosis, preliminary headache, fever, hyperidrosis, acne, and other disorders of the skin; modifications of urine, digestive disturbances, and malnutrition; vasomotor disorders and edema; disturbances of the reflexes; motor agitations which may be cataleptic psychologically; catatonic inertia, negativism or suggestibility, confusion of ideas with or without delirium, erroneous sense perceptions, and ideas of

reference which may lead to delusion formation, either of agitated type with resulting verbigeration or of depressed character leading to stupor.

[Under the title of stupidity or morosity Willis (in 1672) had already observed what was first described and later named dementia præcox by Morel (1851), who had clearly described the suggestibility, stereotypy, catatonia, and the negativism which he called nihilism. He even gives a picture of the typical cataleptic attitude. He also placed it along with the *confusion mentale*, which was then called stupidity.]

Catatonia, like catalepsy, may occur in childhood. It is the commonest form of dementia præcox at that period, perhaps on account of the psychomotor predispositions of the child. Some of the stereotypies of children, which teachers may mistake for imitative grimaces, may be due to a catatonic psychosis. Puberty is shown early in many of these cases.

Loewy had laid stress upon what he calls pseudocatatonic movements, which occur in mild mental cases which do not become demented. One of his cases occurred during an attack of appendicitis. The movements were influenced by suggestion and the patient recovered completely. In Loewy's opinion normal persons may show catatonic types of movement. These cases are probably of the same type, occurring in the course of mild intoxication and infections, as described by Latron.

Two fatal cases of chronic lesion of the left angular gyrus, which had been diagnosed as dementia præcox. These focal lesions of the cortex were associated with late catatonia. One case showed a cyst of softening and the other a solitary tubercle. Both lesions could well be of suitable age to correspond with the date of onset. Decidedly atypical, however, was the age of onset, 41 in

one; 36 in the other. Southard and Canavan (Amer. Jour. of Insanity, Jan., 1916).

**PATHOLOGY.**—Very many catatonics die of tuberculosis or other infections; so that it is very hard to know whether changes in the central nervous system found *post mortem* contribute to the symptoms or whether they are merely the consequences of the poisonous action of the pathogenic organism which has killed the patient. A number of studies of the brain have been made after the death of patients who have shown catatonic phases in their dementia. The findings have been by no means uniform. Thus, Klippel, in 6 cases of dementia præcox, found the chief lesion to be a diminution and alteration of quality of the substance of the cells of the cortex. Lhermitte confirmed this in 2 other cases, but all of these had tuberculous lesions in the lungs. The vast majority of catatonics reveal tuberculous lesions *post mortem*, though not in the nervous system.

Moriyasu (1909) found more widely spread lesions with fibrillary degeneration and reduction in every part of the cortex in small areas, not preponderating anywhere. He did not think that the cellular changes he found differ from those in other psychoses. He found a distinct gliosis around the blood-vessels, which were often thickened and proliferating. Their walls contained mast cells and much pigment. In all his cases, the cells of Clarke's column in the spinal cord, which is the lower center for the control of tonus and attitudes of the muscles, were found. But the cells of the ventral column were also affected.

Mickles's case showed actual adhe-

sions due to chronic meningitis with decortications and a thickened pia-arachnoid. The convulsions, too, were atrophic.

However, at least one undoubted case without visceral lesions has been reported, and this, too, occurred during a convulsive phase of a catatonic. The patient was 31 years old. No parietic lesions were found; but the ventricles were small and the weight of the brain, instead of being 12 per cent. less than that of the cranial contents, was only 1.2 per cent. less. Dreyfus, the reporter, believed that both convulsions and death were due to acute swelling of the brain. This case refutes the opinion of Tetzner, that convulsive catatonia must be epileptic or parietic in genesis. Yet, Nouet and Trepsat (1910) have reported a case of undoubted catatonic dementia in a man of 23 in whom epilepsy appeared simultaneously: Hypertrophy of the adrenals and absence of interstitial cells of the testes have been found in some cases by Laignel-Lavastine (*Jour. de neurol.*, 1908), who thinks that the clinical symptoms strongly suggest perturbations of the internal secretions.

**PROGNOSIS.**—Even though remissions may occur, the ultimate course is apt to be grave, the disorder recurring in at least 80 per cent. of cases, most of which progress to serious dementia in the course of years. The aspect of the malady may, however, change to resemble one of the other forms of dementia præcox, under which head a further discussion of the course of the disease will be found.

**TREATMENT.**—**Confinement** in a special institution is usually impera-

tive, as the patients are always very troublesome and sometimes become suddenly dangerous. Until arrangements can be made, a trained attendant is advisable. Failing this, restraint may be necessary; but continuous immersion in a **warm** bath is very quieting to most cases. Persuasion to overcome the obstinacy is useless.

Very little attention has hitherto been devoted to the occurrence of catatonic symptoms in idiocy, except by Weygandt and Vogt. They are, however, very frequent and striking—stereotypies of speech, movement, and position, catalepsy, and echolalia may all be observed.

According to the author's experience, stereotypies occur almost exclusively in the lower grades of idiocy. Out of 255 low-grade idiots, 152 exhibited stereotypies of one kind or another. The most frequent consisted of rhythmical to-and-fro balancing movements of the body. Catalepsy, echolalia, and echopraxis were observed in 11 cases. Rhythmical phrases or inarticulate sounds are common phenomena in idiocy. Stereotypies of position are rarer than those of movement. When they do occur the similarity to catatonia is very marked.

Sometimes the stereotyped movements involve injury to the patient, *e.g.*, in one of the author's cases, where the forehead was struck rhythmically with the fist, an extensive ulcer has developed over the area affected. By giving the patient a ribbon to hold, his attention could be diverted, and the movement ceased. If the ribbon was removed, however, the stereotypy immediately recommenced. This **diversion of the attention** is to be recommended in all similar cases, and is much preferable to restraint.

The stereotypies displayed by idiots generally cease at once if the patient's attention is engaged by conversation or some other means. The



possibility of thus influencing and controlling the movements is a point of prime importance in the differentiation from catatonia. W. Plaskuda (*Zeit. f. d. gesamt. Neurol. u. Psychiat.*, Bd. iv, H. 3, 1911).

### NARCOLEPSY.

This is a condition of inappropriate and intemperate sleepiness which must not be confused with catalepsy; for it is, although morbid, of the same nature as sleep itself.

**SYMPTOMS.**—The inaccessibility to stimuli of the narcoleptic is only that of profound sleep. The eyes are closed and the eyeballs turned toward the roof of the orbits. The muscles are relaxed without waxy plasticity. Consciousness is as completely suspended as in true sleep, and most patients are incapable of recounting what took place around them during the attack.

Case of narcolepsy in a man of 22 without neurotic family history, but with a personal history of marked nervousness, gastritis and subsequent intemperance, and extreme venery. Hallucinations appeared, and then a tendency to excessive sleep, falling asleep with the greatest readiness and often from 20 to 50 times during the working day. The sleep was never deep; he was always awakened by a touch or a word, and often awakened within a few moments even without being disturbed. H. N. Moyer (*Med. Record*, Nov. 19, 1898).

Case in a boy 17 years of age who for four years had had a marked tendency to sleep during the day, for periods of four or five minutes, remaining asleep sometimes for an hour. He would even fall asleep while walking on the street, while eating, reading, or talking. He slept well at night, his memory was becoming impaired, and there was paresis of the right side of the face. Later he developed some paresis of the hand,

especially after laughing, but as a result of hydrotherapy, galvanization of the head, and hypnosis he improved very rapidly. The interesting feature of this and other cases is the motor inhibition after laughing. Löwenfeld (*Münch. med. Woch.*, June 24, 1902).

Case of a colored man 48 years of age who drops off to sleep for half an hour or so every three hours. The sleep is refreshing, but light, so that no word spoken in his hearing escapes him. He is easily aroused. The naps come on almost instantaneously. There is no drowsiness between the naps, and his awaking is instant and without any confusion or other feeling left behind. There is a history of specific disease at 18. The patient is moderate in all his habits and sexually temperate. Pupils are normal; co-ordination is normal; also the abdominal viscera, and there is no adenopathy. The reflexes show a contralateral disparity, probably due to a past spinal lues. The morbid somnolence can hardly be regarded as hysterical, and a cerebral lesion seems altogether out of the question. A group of symptoms, plus 0.4 per cent. of albumin, with granular, fatty, and epithelial casts in the centrifuged sediment, suggests secondary contracted kidney. Hecht (*Amer. Jour. Med. Sci.*, March, 1908).

In some cases, however, the state resembles that of the waking dream caused by intoxication, the patient being capable of continuing what he is doing without interrupting his sleep.

**Etiology and Pathogenesis.**—That it is of the same genesis as true sleep is probable. But its close alliance at least to the torpor of the confusional states is beyond question. That it is due to toxicosis is most likely. Narcotics, opium, trypanosomiasis, infections, and autointoxications, especially hepatic insufficiency (Ballet and Levi),

may produce it (Régis, Congrès de Bruxelles, 1904).

Case of narcolepsy occurring in a woman 48 years of age. She complained of sleeping frequently in the course of the day, had weakness in the legs, and had suffered for some time from enteritis and metritis. Upon examination it was found that she consumed about 2.5 liters of coffee and 1 liter of tea every day. Guleke (Münch. med. Woch., Sept. 30, 1902).

Case in which not a single symptom could be detected pointing to any of the pertaining and known types of autointoxication, but it by no means follows that the primary cause of this instance of pathological sleep is necessarily also the underlying factor in the production of any or all other cases of morbid somnolence. Heinrich Stern (Med. Rec., Jan. 11, 1902).

Narcolepsy occurs also in secondary syphilis, insolation, and arteriosclerosis. In a case observed by myself the Cambridge pancreatic reaction was present, and the stools revealed undigested muscle fiber two weeks after the last ingestion of meat, the eating of which seemed to greatly favor the attacks.

Narcolepsy is particularly frequent in cases of tumor of the pituitary body. Whether this is due to disordered secretion or to interference with cerebral function by pressure is not certain. In favor of the latter is the fact that somnolence is frequent when tumors are present in other situations, more especially in the posterior fossa; but this, again, may be due to interference with pituitary function by stasis of the circulation of the blood, lymph, or cerebrospinal fluid.

It is significant that growths in the contiguous pineal body also cause somnolence.

The writer has observed that dogs whose thyroid is extirpated are after a time found asleep nearly all the time, and so much so that the loudest noise will not make them stir. Similar effects can also be observed in tumors of the pituitary body, for instance in acromegaly. However, as it has been shown by Gley, Rogowitsch, Stieda, Sajous, and others, the pituitary gland and the thyroid are in a very close relationship, and, as the writer also pointed out in a previous paper, we find pretty constantly alterations of the thyroid gland in acromegaly. Salmon also states that in tumors of the pituitary body, with sleepiness, there was generally found an atrophic condition of the thyroid. Arnold Lorand (Monthly Cyclo. of Pract. Med., April, 1906).

**Treatment.**—The treatment of a narcoleptic case when sleep is inordinately prolonged does not differ from that recommended under catalepsy (*q.v.*). The underlying cause must then receive attention. Dercum recommends **thyroid gland**, preferably small doses at first, but gradually increased. Tea and coffee or even caffeine have been found useless.

In many of these cases the period of sleep is filled with vivid dreams. In this respect they resemble the sleep of neurasthenia, with which, as in a personal case, the hysteria may be associated. In such cases an already exhausted nervous system attempting to recover from an expenditure of energy which it can ill afford seems to be a rational explanation for the prolonged sleep. The treatment of such cases is to change the vicious, deranged metabolism of the individual by eliminating the element of copremia from the overloaded bowel; to change the tone of the muscles, and to correct, as far as possible, by **massage** and **graduated exercises**, the all-important muscle metabolism, and, finally, by complete **rest** and **judicious feeding**, to build up the entire system and, with it, the **ex-**

hausted and deranged nervous system. D. J. McCarthy (*Amer. Jour. Med. Sci.*, Feb., 1900).

Case in a strong, somatically healthy, laboring man 41 years old who suddenly began having attacks of sleep many times a day, evidently involuntary, but unaccompanied by any of the physical signs of illness, even the stigmata of hysteria being absent. There was a slight mental change, the heightened irritability being perhaps not unnatural under the circumstances. His natural sleeping period was undisturbed except by particularly vivid and unpleasant dreams.

The administration of caffeine was of no use in keeping him awake, and his principal treatment consisted in the application of **static sparks** to his head, with suggestion. This, with general hygienic treatment and the **change of scene** and occupation, appeared to be of benefit, as in a week's time the number of attacks daily was considerably diminished. C. D. Camp (*Jour. of Abnormal Psychology*, April-May, 1907).

Two cases of children of 8 and 15 who suddenly dropped to sleep during the day, sometimes ten to fifty or more times. The sleep lasted a few seconds or minutes; it came on without prodrome and the child woke with mind clear. The sleep occurred in one case at about the same hours each day, but in the other at irregular hours. The fear of danger or of punishment sometimes postponed the attacks. Bromides and deprivation of salt had no effect, but marked improvement amounting to a cure to date in one case was obtained with **isolation** and **psychotherapy**. In the elder patient there were indications of angioneurotic edema, and transient hysteric hemiplegia developed later. Both children were girls standing well in their classes, and there was nothing otherwise to suggest epilepsy. Psychotherapy for children must be of the imperative type, Dejerine says; he calls it "school-master therapeutics." The children

are scolded, humiliated, or punished, the appeals being to their pride. Sézary and Montet (*Revue de méd.*, Jan., 1908).

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## CATARACT. — DEFINITION.

—By the term "cataract" is meant an opacity, partial or complete, of the crystalline lens, or its capsule.

**VARIETIES.**—The opacity of the crystalline lens may be (a) primary, or idiopathic; (b) secondary to diseases of other ocular structures, and (c) symptomatic of general disorders.

**SYMPTOMS.**—The objective signs and symptoms vary according to the variety of the cataract, being mainly dependent upon the extent, the character, and the density of the lenticular opacity.

In the immature forms the anterior chambers may be shallower than normal, this being due to a forward protrusion of the iris, produced by a swelling of the lens. In hypermature cataract the anterior chamber may become deep, while in the mature condition it is practically of normal size.

Mere inspection of the pupil without the aid of oblique illumination does not always give conclusive evidence in regard to the presence of cataract; yet, generally, especially in fairly advanced cases, the pupillary area assumes a dull-gray or glistening-white appearance, according to the age and the character of the lenticular opacity, a condition, however, which needs careful clinical confirmation before any certainty as to diagnosis can be vouchsafed. At times the pupil may appear almost entirely black or brown in tint. In some, particularly indeterminate cases

of this type, the catoptric test is of value. Very rarely, glistening polychromous, crystalline masses may stud the pupillary area.

Study of the eye-ground in the incipient stages will frequently, especially in comparatively young and ametropic subjects, reveal coarse local changes connected with the uveal tract. In all cases, except when contraindicated, and in all stages, mydriatics should be resorted to, to make as thorough a study of the intraocular conditions as possible. Vision is always disturbed to a greater or a less degree, according to the situation, the extent, and the nature of the opacity.

The subjective signs are fairly constant in all forms of cataract. Large, circumscribed, peripherally seated opacities are much less disturbing to sight than small ones, or even faint nuclear hazes situated opposite the pupillary area. Nearly always during the formative period, "motes," "veils," and "cobwebs" are spoken of, while at times multiple and distorted visions are the chief complaints. As the lens becomes more opaque, however, the sight becomes more and more reduced, until, eventually, large objects can no longer be discerned, although, if the condition be uncomplicated, the distinction between light and darkness remains.

During the incipient stages of cataract, it frequently happens in the aged that they are able to dispense with lenses ordinarily used for near-work, and, at times, desire concave ones for distant vision. This, which is due to an increase in the refractive power of the eye, consequent upon swelling of the lens, before any opacity makes its appearance, is known as "second sight." Pain and

photophobia, which are best relieved by smoked glasses, are rather infrequent symptoms in the early stages of the condition, and are referable to the pressure of the swollen lens on the ciliary body and the iris.

A cataract may remain permanently limited to some particular portion of the lens, or it may gradually involve the entire lens substance and lead to practically complete opacification.

The former variety, which is divided into several types, dependent upon the locality of the lens which is involved, may be either congenital or acquired. When the opacity is situated in the anterior pole of the lens, the condition is known as

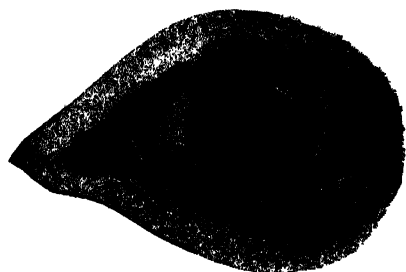


Capsular cataract. (Becker.)

anterior polar cataract or anterior pyramidal cataract. The cause of the congenital form is supposed to be due to some fetal disturbance operating during the development of the lens. In the polar variety, which, in reality, is one of the true cataractous forms, the opacity assumes the figure of a star or rosette, with its radii extending toward the periphery. It has been seen to follow contusions of the globe, to appear as a part of so-called pigmentary retinitis, and exhibit itself as a consequence of uveitis. The postnatal form, as a rule, is the permanent result of rupture of a corneal ulcer, by which the anterior capsule of the lens is brought into contact with the inflamed cornea, leading to proliferation of the epithelial cells of the lens occupying the position of the pupillary area, with the formation of

a subcapsular opacity after the re-formation of the anterior chamber; this being in addition to the nebule, which, as a rule, but faintly marks the site of the previous corneal ulceration.

When there is a deposition upon the anterior face of the capsule which in



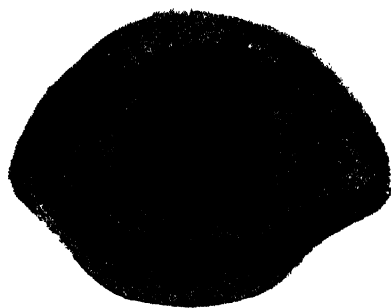
Posterior cortical cataract. (Siehel.)

itself is irregular, opaque, and thickened directly beneath, the condition is known as anterior pyramidal cataract; in reality it is situated in both the lens and its anterior capsule. The disturbance in vision depends upon the extent, position, and density of the opacity. Treatment, as a rule, is unavailing, except the possibility of an optical iridectomy should the opaque area be large and the pupil small.

When the opacity is situated at the opposite pole of the lens, the condition is designated as posterior polar cataract, or posterior pyramidal cataract. In most instances the latter form is congenital in type, and is due to some interference with the disappearance of the hyaloid artery. It is recognized as a small dot or area on the posterior capsule at the posterior pole of the lens, projecting backward into the vitreous humor. True posterior polar cataract is, at times, found as the initial point of election of the senile form, and is not infrequently

seen associated with uveal disorder associated with lymph-stream disturbance and liquefaction in the vitreous chamber. Generally it appears in the stellar form. In this variety interference with vision depends not only upon the size of the opacity, but also upon concomitant and relevant changes. Treatment, to be of any avail, must be directed, if possible, toward any existing cause.

A third form, although separated into quite a series of groupings, consists of localizations in various parts of the lens. Opaque stripes extending from pole to pole, and often combined with the central and the zonular forms, are known under the name of "spindle-shaped" or "fusiform" cataract. Minute dots, usually mostly situated in the central portion of the lens, and frequently grouped in the anterior cortex, are known as "punctate cataract." Small spheroidal opacities in the nucleus, of congenital



Congenital cataract with riders. (Siehel.)

type, have, by some, been described as "central cataract." As a rule, they are all mere concomitants of gross intraocular pathological change.

Zonular opacities situated between the nucleus and the cortex of the lens, both of these portions being transparent, are not uncommon. At times they may progress as a series

of minute opaque processes, or "riders," as they are termed, rendering the lens quite opaque. This variety of cataract, also known as "perinuclear" or "lamellar," is either congenital or forms during infancy in rachitic subjects or in those who have been affected with convulsions. Usually it is binocular, and almost without exception is but slowly progressive, though cases in which it has become total have been reported. On account of the situation of the main opacity or opacities, vision is usually markedly disturbed, necessitating either artificial mydriasis, iridectomy, or lens removal.

If the appearance of the lens shows that the opacity is probably stationary, and if the opaque zone be not so broad that, after the pupil has been dilated with a mydriatic, vision is bettered, it is advisable to expose a portion of the transparent periphery of the lens by an iridectomy, thus obtaining an eccentric pupil through which the subject can look. If, on the other hand, the peripheral zone of transparent lens matter be narrow, and if there be evidences of increase in the cataract, it is preferable to remove the lens, either by extraction, when the nucleus is well hardened, or by discission, when the lens matter appears soft.

**Traumatic Cataract.**—As a rule, this form of lenticular opacity is the result of a rupture or a disturbance of the capsule of the lens from an injury which permits the aqueous humor or vitreous humor to come into contact with the lens fibers. The laceration in the capsule may be the result of either direct injury from penetration of a foreign body or indirectly by contusion.

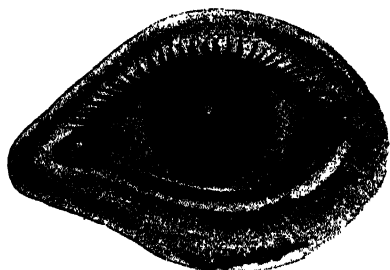
Case of a youth who had been injured three months before by a blow from a stick, which penetrated the cornea and lens capsule. In the first three weeks following the accident there was considerable swelling of the lens, but increase of tension was combated by spontaneous opening of the corneal wound from time to time during this period. Then the anterior chamber closed, the eye got quiet, and absorption of the cortex proceeded satisfactorily. Anterior synechia developed at the site of the corneal wound, making the pupil somewhat irregular. Considerable opaque anterior capsule and a moderate amount of unabsorbed cortex were visible. Iodine powder was being dusted into the eye daily. W. A. Sedwick (*Jour. of Ophthal. and Otolaryn.*, Dec., 1909).

In case of a traumatic cataract, if the patient is seen immediately or soon after the injury, after recovery from the shock and before the local reaction has made careful work almost impossible, the lens should be extracted. This can be done under local anesthesia, though a general anesthetic is preferable in many cases. If local reaction is already marked, one should wait from four to six days, when it subsides, and then remove the lens before the secondary inflammatory symptoms have become severe. A general anesthetic is then necessary. J. A. Donovan (*Jour. Amer. Med. Assoc.*, July 15, 1911).

Case of a boy aged 8 who, while playing with other small boys, one of whom had an airgun, was struck in the right eye by a B.B. shot fired at a distance of about twelve feet. Inspection of the eye revealed slight ciliary congestion. The cornea was not perforated, but showed slight haziness toward the inferior temporal quadrant; there was slight hyperemia and the pupil was moderately dilated. Six weeks later the cornea was clear, but in the inferior temporal quadrant of the lens there was a distinct round opacity about 2 mm. in diameter and involving the anterior layers of the

lens. Vision at this time was 2/200. Ten weeks after the injury the lens was completely opaque.

Opacity may be partial and become stationary, or it may progress and become complete. It is not necessary that the blow should fall on the eyeball directly. A blow on the orbit or side of the head may be followed by opacity of the lens. Weeks reports the case of a patient, 25 years old, thrown from a carriage, striking on the right side of the head. Some months later vision in the right eye became impaired. Examination revealed the presence of minute opaque spiculæ at the periphery of the lens, extending from the equator toward



Congenital, nuclear, and perinuclear cataract.  
(Sichel.)

either pole. The center of the lens remained free. Fifteen years later the opaque striæ had not materially changed. Fuchs reports the clearing up of four traumatic cataracts. Lauder (Cleveland Med. Jour., Oct., 1911).

Shortly after the capsular laceration the lens fibers near the rent begin to swell and cloud. Later, if it be the anterior capsule that is injured, they ooze out into the anterior chamber, appearing as gray, fluffy-looking masses. The aqueous humor, however, soon dissolves the lens material which has gotten into the anterior chamber and thus, gaining freer access to the interior of the lens by the removal of the primary plugs of lens matter, causes more or less of

the lens substance to become swollen, opaque, and absorbed. In this way, after the lapse of some time, the major portion of the lens substance may be dissolved and the pupil again become almost black. In most cases, however, the capsular wound cicatrizes and becomes closed, stopping the process of absorption before the removal of all of the lens material by the liquefying method is fully accomplished.

Many cases of traumatic cataract pursue their course with but few signs of inflammation; but a successful termination is often prevented by the development of an iritis caused either by direct injury or by pressure of loose or swollen lens matter. Septic matter may be also introduced into the eye, either at the time of the traumatism or later, giving rise to an iridocyclitis, a panophthalmitis, and even an orbital inflammation. If not prevented, it not infrequently happens that secondary glaucoma supervenes. This condition is generally due to either a blocking of the angle of the anterior chamber by pressure or the presence of a mass of lens matter obstructing the passage of the aqueous humor through the circumlental space, the pupillary area, or the spaces of Fontana.

The increasing forms of cataract are roughly divided into four stages. As a rule, they begin in isolated areas, but increase and multiply until practically all of the lens substance is affected. The most frequent variety is that known as "senile cataract."

In the first, or incipient, stage the opacities usually begin in the periphery of the lens. They appear either in the form of spots or of striæ, which radiate from the lenticular

equator toward the center of the lens. This condition is known as "cortical cataract." In other cases the nucleus of the lens becomes quite hazy and opaque, while the periphery may remain comparatively clear. This variety is ordinarily designated as "nuclear cataract." In most instances, however, the two forms, in which both the cortical and the nuclear portions of the lens are affected, are associated.

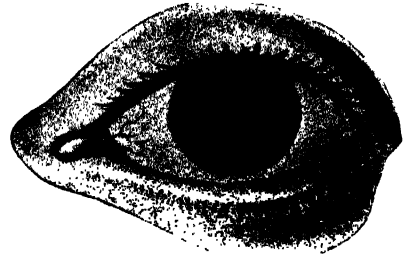
Clinically, in the stage of development of the cataract, the anterior chamber will be found but slightly shallowed or of normal depth, and the opacities will, by oblique illumination, appear as white or gray streaks and sectors with dots.

In the second stage, or that of ripening, the lens is swollen, this being due to the fact that it contains an increased quantity of fluid. The opacities are more pronounced, while numerous clear spaces are scattered throughout the lens substance. As a rule, the anterior surface of the lens has an iridescent, bluish-white appearance. The anterior chamber is shallow. Clear spaces situated in the lens between the iris and the opaque portions of the lens substance can be recognized by oblique illumination, allowing a shadow of the iris to be cast upon the lens at the side from which the light is thrown.

In the third, or mature, stage the lens has returned to its normal size, this being, in great measure, due to the loss of the lenticular fluids by resorption. The clear spaces in the lens substance are replaced by opacities, and the anterior chamber has regained its normal depth. The iris fails to cast a shadow. The lens presents a dull-gray or waxy appear-

ance, and its anterior face is seen to be situated on a level with the pupillary margin of the iris. Should the pupil be artificially dilated, it will be found that the red reflex from the fundus, which can be dimly obtained while the cataract is in its immature stage, is lost.

In the fourth, or hypermature, stage, as a rule, one of two changes occurs: either the cortical substance disintegrates and becomes fluid, while the nucleus remains hard,—so-called "Morgagnian cataract,"—or the broken-down cortical substance becomes



Well-advanced cortical cataract. (Siehel.)

more greatly inspissated and dries into a hard and somewhat flattened mass.

In hypermature cataract the anterior chamber is of normal or of increased depth, the iris fails to cast any shadow, and the surface of the lens appears either homogeneous or exhibits irregular dots in the situation of the ordinary physiological sectors. If, however, the overripening process be more advanced, fatty and calcareous degeneration occurs in the lens and its capsule, the anterior chamber becomes deeper than normal, and tremulousness of the iris can be seen.

In Morgagnian cataract the nucleus may sink to the bottom of the liquid contents contained within the lens



capsule, the walls of the capsule may come in contact with one another, and the volume of the lens mass become increasingly smaller until nothing but a thin, transparent membrane remains,—so-called “membranous cataract.”

Practically, according as the dimensions of the nucleus of the lens vary, a cataract is spoken of as “hard” or “soft.” When there is no hard



Section through Morgagnian cataract. (Recker.)

nucleus the cataract is said to be soft; so that, as a rule, all cataracts occurring in persons under 35 years of age fall under this category. In older subjects, however, the lenticular nucleus is larger and more or less sclerosed; so that opacities occurring in such persons are designated as hard cataracts, although the cortices of such lenses may be quite soft.

In some senile cataracts the general sclerosis becomes so pronounced that practically the entire lens is involved in it. In such a condition the cataract, as a rule, appears of a dense red-

dish-brown tint, and is markedly translucent. This variety, when complicated with the remains of old hemorrhagic extravasations, is usually termed “black cataract.”

**Secondary Cataract.**—This improperly termed condition refers to the changes that are, at times, observed in the capsule of the lens following, for example, extraction of the lens. It is frequently seen after the attempted removal of an immature cataract in which a portion of the lens substance remains. This occurs when the capsular membranes become agglutinated and the escape of any remaining lens material is prevented. In many instances it happens that the entire pupillary area is not covered by the opacity, and fairly satisfactory vision may be obtained.

When the condition does not develop until some months after the primary operation for extraction, it is generally dependent upon a fresh proliferation of the epithelial layer, with reduplication of the capsular remains.

**ETIOLOGY.**—Congenital conditions operating upon the causation of cataract, which, at times, based upon well-founded clinical observation, have been determined to be hereditary in type, practically resolve themselves either into developmental disturbances in the eye or antenatal inflammatory reaction of the organ.

Instance of a family in which 5 members are affected by a very definite and peculiar variety of congenital cataract similar to that described by Nettleship and Ogilvie the previous year. The family consists of a man, his wife, 5 sons, and 1 daughter; the persons known to be affected are the father, the third, fourth, and fifth sons, and the daugh-

ter. Burton Chance (Trans. Amer. Ophthal. Soc., vol. xi, pt. ii, 1907).

Genealogical tree showing predilection to cataract in 275 persons, all descended from 2 brothers. The chart, divisible into two parts, shows that the larger part (about 180) contained numerous cases of lamellar and Coppock cataracts, and the smaller 32 cases of cataract and 15 of retinitis pigmentosa out of the total of 150. The presence of these two conditions associated in the same genealogy is doubtless due to each disease having been introduced by different ancestors from independent sources, and the fact that the retinitis pigmentosa is found only in the descendants of 1 brother inclines one to assume that the taint has been introduced through the wife. The pedigree also shows that Coppock cataract can develop in a child from a parent with lamellar cataract. E. Nettleship (Jour. of Ophthal. and Otolaryn., Aug., 1908).

The writer found cataract in 100 per cent. of the litters of living young animals (in eight experiments). They were produced by intoxicating pregnant rabbits with naphthalin. Ten different kinds of ocular malformations were produced by feeding naphthalin to rabbits and guinea-pigs: coloboma of iris and choroid, persistent hyaloid artery, posterior lenticonus, coloboma of lids, microblephary, etc. The experiments shed the first light on the casual genesis of malformation in vertebrates and repudiate the prevalent opinion that all ocular malformations are due to an anomaly of the germ and heredity. H. E. Pagenstecher (Ophthalmology, Oct., 1911).

Family in which cataract affected four generations, but only the female members, while the male members had absolutely normal eyes. Among the members of the family no inter-marriages had occurred; syphilis or rachitis could be positively excluded. Hilbert (Münch. med. Woch., June 4, 1912).

The Volkmann family was studied by the writer who traced the tendency to zonular cataract through 4 generations. The cataract was bilateral in nearly all those affected. Its occurrence did not indicate that it was inherited as a mendelian dominant, but on the other hand there was nothing positive to disprove this. Epilepsy and idiocy were not unusually common in this family, but the poor eyesight reduced the level of the environment. Of the 60 children or young persons in the various branches of the family, 25 had cataract. K. Lehmann (Ugeskrift f. Laeger, Sept. 12, 1918).

General disease, independent of senility, particularly if of vascular or lymphatic type, becomes, at times, a causative factor. In these cases there is an imperfect abstraction of auto-toxic substances: the fact that subjects with increased blood-pressure are more prone to the condition than those with normal vascular tension illustrates this very well. Diabetes mellitus is responsible for about 1 per cent. of cases, this variety being bilateral and developing rapidly. Rachitis, nephritis, and some affections of the skin are credited with the production of the condition.

The thyroid gland is now generally recognized as contributing an internal secretion to the body. Any disturbance of this function produces an autointoxication, which frequently causes, among other results, changes in the nutrition of the crystalline lens. After a detailed review of the literature, the author gives his own experiences, which embrace 28 cases of cataract with struma. All the cases were in females, in 22 of whom bilateral cataracts developed. The goiter was usually of considerable size, often produced marked stridor by compression of the trachea. The cataract in these cases does not usually include the whole lens; it involves chiefly the nuclear zone and

the perinuclear layers. The outer cortex, which is usually opaque in senile cataract, is quite clear in these cases, or, at most, exhibits a few punctiform or linear opacities. A thorough examination of the body, including the urine, revealed no other possible cause for the cataract in these patients. A. Vossius (*Zeit. für klin. Med.*, Bd. lv, p. 63, 1905).

Arteriosclerosis and age are no longer synonymous conditions, because the former occurs in the young as well as in the old. Any acute infectious disease may leave its imprint on the blood-vessels and eventually, when given proper impetus, terminate in arteriosclerosis, either local or general. Ordinary senile cataract is an expression of arteriosclerosis, the result of malnutrition and local autointoxication. Opacities begin in the lower part of the lens, probably the result of gravity, and disseminate from below upward. In glaucoma, the arteriosclerotic process goes on in the posterior part of the globe, with marked changes even in the ophthalmic and retinal arteries. G. F. Suker (*Jour. of Ophthal. and Otolaryn.*, April, 1908).

Study of 400 inmates of the National Military Home at Dayton, all over 60 years of age, with special reference to the influence of arterial sclerosis and high blood-pressure in the etiology of cataract. The writer places the upper limit of normal blood-pressure for men of that age and condition in life at 160 mm. Hg, all above that being pathologic. With normal pressure he found in 59 men, between 60 and 65 years old, 37.3 per cent. of cataract; in 79 men, between 65 and 70, 41.8 per cent.; in 35 men, between 70 and 75, 54.3 per cent.; in 20 men, between 75 and 80, 70 per cent.; in 4 men, between 85 and 95, 75 per cent. With pathological pressure he found in 57 men, between 60 and 65 years of age, 42.1 per cent. of cataract; in 61 men, between 65 and 70, 54.1 per cent.; in 44 men, between 70 and 75 years, 55 per cent.; in 22 men, between 75 and 80,

68.2 per cent.; in 12 men, between 80 and 85, 83.33 per cent., and 1 man, 95 years old, also had cataract, thus showing a steady rise in the frequency of cataract with age, which was greater with pathological than with normal blood-pressure. The statistics further show that 79.5 per cent. of the 400 men had blood-pressure between 130 and 180 mm. Hg, and the largest number of cataracts were found between these limits of pressure. For example, 79 men, between 65 and 70 years old, had 33 cataracts (41.8 per cent.), with a pressure under 160; 61 men, between the same ages, had 33 cataracts, or 54.1 per cent., with a pressure 160 mm. Hg or more. The statistics also show that an increase in pressure of 41.4 mm. in the pathological over the normal class is accompanied by an increase of 17 cataracts, or 18.3 per cent.

It is evident that pathological pressure, or the conditions leading to it, have considerable influence in causing cataract. Burge, working under the direction of Howell, of Johns Hopkins, has reported finding "a marked decrease in the potassium and a corresponding increase in the calcium salts" in the ash of cataractous lenses, a fact suggestive that such increase of lime salts may be a factor in the process leading to aging and arteriosclerosis, an idea which he believes has long been entertained. D. W. Greene (*Jour. Amer. Med. Assoc.*, Aug. 1, 1911).

The influence of heredity is well shown by the Volkmann family, which showed zonular cataract in 4 generations. It was bilateral in nearly every instance. Its occurrence did not indicate that it was inherited as a mendelian dominant; but there was nothing positive to disprove this. Epilepsy and idiocy were not unusually common in this family, but the poor eyesight reduced the level of the environment. Of the 60 minors in the various branches of the family, 25 had cataract. K. Lehmann (*Ugeskrift f. Læger*, Sept. 12, 1918).

Certain drugs, such as ergot and naphthalin introduced into the system, are eminently causal in character.

Local diseases and traumatism frequently produce all forms and varieties, especially in subjects in which there are changes affecting the lymph-stream formation and circulation, and where the solvent power of the lymph-fluids can be made to exert their influence directly upon the unprotected and exposed fibers themselves.

Constant direct exposure of the eye to high degrees of heat, such as among glassblowers and puddlers or those who are subjected to continued undue action of X-rays, ultraviolet or chemical rays, will not infrequently give rise to the condition.

It has been asserted, especially by the Germans, that cataract is of frequent occurrence among glassworkers, it being sought to connect this with the powerful heat and the sweating which accompanies it. The writer investigated the question in Sheffield—a large bottle-making district—and concludes that such workers are no more subject to the affection than those employed in other trades. Snell (*Brit. Med. Jour.*, Jan. 5, 1907).

In those parts of India where light and glare are intense, cataract is very prevalent. The position of the opacity in glassblowers' cataract suggests that light may be the cause of this form of cataract. Cataract has not been artificially produced by sunlight. Cataract has been artificially produced by electric light in animals. Exposure to intense electric light in man does not produce cataract. No reliable case has, up to the present, been recorded of the production of lens opacities by the ultraviolet rays. The inhabitants of mountainous regions, where ultraviolet rays abound, would, if these rays were the cause of cataract, be the greatest suf-

ferers, which is not the case (Birch-Hirschfeld). Intense dry heat prevails in those parts of India where cataract is common. Direct heat has not been proved to produce cataract. Glassblowers' cataract can be as well explained by a heat as by a light theory, as both conditions coexist. Pisani (*Brit. Med. Jour.*, Oct. 29, 1910).



Formative changes in a degenerating lens.  
(Becker.)

At least 2 factors should be considered in the genesis of cataract, one a modification of the protein of the lens by ultraviolet radiation, and the other certain inorganic salts by which the modified protein can be precipitated. According to this hypothesis the prevalence of cataract among people living in the tropics could be accounted for by the increase in the radiant energy factor modifying the lens protein so that an excess of salts, such as silicates in case of people in India, would combine with the protein to precipitate it and produce an opacity of the lens or cataract. The prevalence of cataract among glassblowers is also accounted for by the excess of the

radiant energy factor, the assumption being that glassblowers who acquire cataract have a more or less disturbed condition of nutrition expressing itself in an increase in sugar in case of diabetes, calcium salts, or some other substance, which can combine with the lens protein made sensitive by the action of the short wave lengths. The prevalence of cataract among diabetics is due to the chemical factor. W. E. Burge (*Archives of Ophthal.*, Jan., 1918).

Lightning and electricity have also caused cataract in a small proportion of cases.

Case of a soldier who was struck by lightning and rendered senseless for a while. After recovery he felt perfectly well, with the exception of a burning and redness in the left eye. The discomfort persisting, he entered the hospital a week after the accident, where a diagnosis was made of conjunctivitis. After treatment of boric acid and rest for eighteen days, the patient was discharged cured. Gradually, however, he noticed diminished vision, first in the left and then in the right eye, and at the present time cataract of both eyes is very evident. It is not to be denied that this is the effect of the lightning. Some authorities consider the condition due to shock, others to the heat or to the chemical action (electrolytic) developed by the electric spark. By electric shocks in animals Hess has caused death of the capsular epithelium, with cataract as a result. Francesco Gozzano (*Giorn. Medico del Regio Esercito*, Feb. 28, 1902).

Extraction of a black cataract from a woman aged 71. During the fall of 1895 she stepped into the back yard during a thunderstorm and was momentarily stunned by a flash of lightning, from which she soon seemingly recovered, but that night she was stricken with hemiplegia involving the right side. The remainder of the fall and succeeding winter she was confined to bed, helpless. With the coming of spring she grad-

ually recovered the use of her limbs, and at present there is not the slightest indication that she ever had paralysis, save in the cataract subsequently removed. Smith (*Ophthalmic Record*, Oct., 1906).

Three cases of opacities in the crystalline lens caused by electricity, and which closely resembled cataracts due to lightning. In the first case there is a complete loss of vision, and the only abnormality in the eyes is a cloudiness of the anterior portion of each lens, the cloud resembling small dust particles just under the anterior capsule. In the second case numerous spots appear in the anterior surface of the lens, just under the capsule, and composed of dots and interlacing lines. The fundus was normal and vision equaled 8/10. The third case was similar to the second. The current causing these lesions was an alternating one of 20,000 and 30,000 volts. Stillson (*N. W. Med.*, Feb., 1907).

Case in which cataract followed a stroke of lightning a few months before. The writer cites 39 such cases and concludes that the immediate cause of the lenticular opacity is not due to any particular light rays, but to a direct injury to the capsular epithelium and the lens substance followed by death of the cells. Wolf-  
raun Braun (*Inaugural Dissertation*, 1911; *Ophthalmology*, July, 1911).

Case in which an electric current of 6500 volts passed through the head and produced, five months later, cataract in one eye in the form of delicate black spicules in the lens, with general cloudiness of the media. Four months later the same condition appeared in the other eye. Brandes (*Trans. Belg. Ophthal. Soc.*, Nov. 26, 1911).

**PATHOLOGY.**—By most recent authority, cataract is said to be, as a rule, caused by a too rapid sclerosis and shrinkage of the nucleus. As one of the results, a cessation in the growth of the surrounding lens fibers

takes place. These separate from one another at certain places, especially in the area between the nucleus and the cortex, and particularly in the equatorial region of the former, producing fissures or cavities that gradually become filled with an albuminous liquid, which coagulates and produces spheroidal bodies known as the spheres of Morgagni. Later, the lens fibers which constitute the walls of the fissures become translucent and unequally swollen, giving rise to large and mostly nucleated vesicles of varying sizes and shapes. After a total disintegration of these fibers and cells with their remains has fairly well taken place, the epithelium of the lens becomes abnormally thickened, the most peripheral lens fibers become vacuolated, and the capsule of the organ becomes abnormally separated by the pathological processes at work. In contrast to this breaking down of the cortex, the shrunken and hardened nucleus, as a rule, remains practically unchanged.

**PROGNOSIS.**—The diagnosis of cataract being once established, it frequently becomes necessary to be able to decide how long it will take for the cataract to become mature, or what is known as "ripe." This is difficult, as the rate of progress is variable. Senile cataracts may require years to become sufficiently opaque and hardened for operative interference, while in a few rare instances they have ripened overnight. It is generally wise, therefore, if the incipient signs of cataract be discovered in elderly persons, not to alarm them by telling them of its existence, as vision may not be seriously disturbed for a long period of time. Particularly is this so in nervous females in frail health.

Under all circumstances, however, it is better that the diagnosis be communicated to some responsible friend or relative of the patient. At times, among men, especially those who are harassing themselves with monetary and business affairs, it is best to acquaint them with the nature of the disturbance in order that better hygienic living may be obtained, and proper arrangement of business affairs consummated.

As a general rule, cataracts in the young, those due to general dyscrasia, and the secondary types all develop rapidly. On the contrary, all forms of opacity which commence in the periphery as narrow radii are slower in extension than those in which there are dot-like and broad opacities.

In reference to the prognosis of the result of operative interference for the removal of cataract, numerous factors must be taken into consideration. In many cases it is essential to determine the probable condition of the interior of the eye by means of the so-called candle test. No matter how dense a cataract may be, a patient with a healthy fundus should be able to recognize the position of a localized glare of a candle light placed in all parts of the visual field while the organ is constantly directed toward a second candle flame situated at a central fixation point. If the moving light be lost at any point in the field, a disturbance of one or more of the ocular tunics or some sentient area of the visual apparatus may be diagnosed with almost certain precision, and the prognosis rendered relatively unfavorable. If all light perception be lost, operative procedure would be useless. The condition of the appendages and adnexa of the eye must be

noted, and any disease of them should be carefully treated and removed as much as can be.

The state of health of the patient should be good as possible. General dyscrasia, such as diabetes, rheumatism, syphilis, and old age do not contraindicate operative interference, although their active expressions should be removed in order to render the chances of a successful termination more certain.

Diabetes and other diseases seriously influence the prognosis. Before attempting to operate, the general condition should be improved to the greatest possible extent; increasing debility, tuberculosis, hemorrhage in the retina, and neuroretinitis all contraindicate intervention. The diabetes modifies the tissues, rendering them more liable to infection and prolonging healing. In 1 case the cicatrix left from the operation ruptured five weeks after it had apparently healed. The writer has also witnessed the development of hypostatic pneumonia after the operation. Another serious complication which he has encountered a number of times is a postoperative psychosis. Accidents of this kind, he asserts, are peculiarly liable in diabetics, who generally combine the baleful factors of age, autointoxication, and atony of the intestines. In 1 of his cases the psychosis did not occur for some time after the cataract operation, but then severe neurasthenia developed, accompanied by transient delirium; the patient refused to conform to the dietetic regulations and died in diabetic coma. At the same time, these serious complications of cataract operations are rare; in the majority of cases the results are excellent, but it is necessary to weigh the pros and cons, commence with iridectomy, and redouble the precautions at the time and afterward. De Lapersonne (*Presse méd.*, Feb. 5, 1910).

Diabetic cataract should not be operated on without letting the patient or the relatives understand that even if a good result is obtained the patient will probably not live more than a year or so to enjoy it. The danger of a bad result is much greater than in ordinary cataract, and it involves some danger to the patient's life. If a good result is obtained in one eye, it is unjustifiable to operate on the other eye. **Cocaine hydrochlorate** is advised for local anesthesia, in 3 to 4 per cent. solution. In exceptional cases, **chloroform** is employed. Trimming the lashes, or even epilation, is practised by many, but the writer does not consider these procedures necessary. H. Gifford (*Ophthalmic Rec.*, May, 1911).

Profound anemia, depressed mental conditions, and pulmonary complications are all apt to militate against operative success, which should not be considered as such until at least six months after the procedure.

The writer emphasizes the importance of medical treatment for certain cases of cataract before and after operation. A senile cataract patient is not likely to be in good general condition; while age alone cannot be regarded as a cause, certain nutritive changes to which we can attribute the oncoming of senility predispose to cataract. The writer would have a patient in the hospital from twenty-four to forty-eight hours before operation, or long enough to estimate the physical condition, **unload the bowels** thoroughly, and **reduce blood-pressure** if possible. The individual should be on light **diet** for several days before and should have a good night's rest before the operation. He should be free from other eye troubles. Rheumatism and gout, while important before operation, are most important afterward as an indication of metabolic disorders of autointoxication, which form the principal subject of the paper. D. W.

Greene (Jour. Amer. Med. Assoc., Dec. 2, 1911).

The surroundings of the patient, the character of the place of operation, the time of year, and the hour of the day must all be taken into consideration. The more aseptic the conditions under which the operation is to be performed, the greater are the chances of a successful termination; in fact, this is the greatest of all the prognostic factors. Operations performed in hospitals are much more certain to have a good outcome than those that are performed in private houses.

In regard to the effects of the character and the condition of the cataract itself upon the prognosis, the general rule is that the more nearly mature the cataract is, the more certain are the chances of resultant good vision. In some very old subjects, where the nucleus of the lens is large and well sclerosed, extraction may be made with every chance of eventual excellent result. Operations upon overripe cataracts are not apt to be very successful.

The relative frequency of "fluid vitreous," the degenerate condition of the zonule, and the density of the capsule, with the possibility of the production of secondary glaucoma, are all serious complicating conditions.

**TREATMENT.**—The removal of cataract can be secured only by operation. The fact that a few undoubted instances of spontaneous disappearance of the condition happened does not militate against the force of this statement. Reported instances of its cure by means of drugs or by massage are misleading, and usually emanate from persons or institutions devoted to the purpose of mere monetary gain.

**Case of spontaneous cure of cataract** in a man aged 73, who had repeated attacks of iritis in both eyes. About 40 years earlier he developed cataract of both eyes, the right being worse; this was operated upon with good result. For years the vision in the left eye was such that he could only tell light from dark.

In the left eye, which he believed to have a cataract, there was a deep anterior chamber, tremulous iritis, a small central pupil but no sign of cataract. The lens was obviously dislocated and floated across the pupillary area on movements of the globe. There was no history of injury to the eye, but about 10 years before, the patient had had a severe fall on the back of his head. C. Higgs (Lancet, exciv, 296, 1918).

It is probable that the temporary visual improvement which is, at times, obtained by such patients is due to the instillation of a mydriatic, for, if the opacity be central, dilatation of the pupil may be rendered sufficiently large to remove the iris from before the clear periphery of the lens, thus permitting vision through the unobstructed portion of the lens. Unfortunately, however, the improvement, which, at best, is but temporary, lasts only during the time of the effect of the drug. **Potassium iodide** however, has been recommended by reputable writers: Badal, Leprince, Verderau, and others.

The writer reports favorable results from subconjunctival injection of a 1 per cent. solution of **potassium iodide** containing 2 per cent. **sodium chloride**, in the earlier stages of cataract. Experimental research has also confirmed the benefits of this treatment and explained its mechanism. Since Badal's first recommendation of potassium iodide for this purpose, in 1901, 239 cases have been published, including the writer's own experience with 55, and Verderau's



with 48. Improvement was marked in all but 14 and 6 patients, respectively, and the cataract did not progress in any instance. Badal and his followers merely instill and bathe the eye with 0.025 and 2.5 per cent. solutions, and the results are not so good as with the subconjunctival injection. It is well to commence with their technique, however, and resort to the injections if improvement does not become evident under the instillations. Von Pflugk (Medizinische Klinik, Feb. 16, 1908).

Case of spontaneous absorption of incipient cataract, situated in the center of the lens close onto the anterior capsule, occupying nearly the whole surface of the lens. There being a rheumatic history, sodium salicylate was given, but without effect; then, later, **potassium iodide**, 5 grains (0.3 Gm.) three times a day. **Galvanism** was applied to the eye, about 12 milliamperes for two minutes, which causes a reaction, the eye beginning to water. One month later examination of the eye under homatropine showed a perfectly clear lens of the left eye; the fundus could be seen easily, and retinoscopic shadow was as marked as in the other eye. The patient took 10 grains (0.65 Gm.) of **potassium iodide** daily, and was dieted as a rheumatic, abstained from alcoholic liquors, and did not smoke. S. Moskowitz (N. Y. Med. Jour., Jan. 9, 1909).

In many cases of cataract, central opacity of the lens precedes cortical involvement. If the pupillary aperture be narrow, as is generally the case in the aged, vision is greatly interfered with by such central opacity, which blocks the entire pupil, and where the condition is bilateral the patient is unable to read or write. The operation of preliminary iridectomy usually performed under these circumstances may be impossible for two reasons: 1. General disease contraindicating operation. 2. Refusal of the patient to be operated. For several years the author has successfully used in these cases **euph-**

**thalmin hydrochlorate**, which, by its mydriatic effect, permits of vision through the uninvolved cortical portions of the lens. A mydriatic used for such a purpose must be shown to be entirely harmless, since it may have to be used for several years. A. Dufour (Revue méd. de la Suisse Romande, Jan. 20, 1910).

Cataract in the aged should not be considered a normal senile change, but a manifestation of some pathological process in the uveal tract, the ciliary body, or choroid, whether it is shown by other symptoms or not. By stimulating the lymphatic circulation of the globe by the systematic use of **dionin drops**, or a sufficiently strong subconjunctival injection of **cyanide of mercury**, an artificial sclerosis of the lens is accomplished which causes the disappearance of the fine dust and the arrest of cataract. He contends that this cures some low grade perversion of the function of the ciliary body, which has to do with the nutrition of the lens. Where there is no perversion of the nutrition of the lens neither dionin drops nor subconjunctival injections show any tendency to induce sclerosis. The solution generally used is 8 grains (0.51 Gm.) of dionin to ½ ounce (15 Gm.) of cyanide of mercury solution 1:1000, three drops in the eye at bedtime. As many eyes get very red and some chemosed from these drops, bedtime is preferred for use, so that these effects may pass off during sleep. E. L. Jones (Annals of Ophthalm., Jan., 1916).

To dissolve senile cataract in its early stages the writer commonly uses the following formula in the first week:

*R Sodii acetatis,*  
*Sodii citratis,*  
*Sodii chloridi.* āā gr. xl (2.6 Gm.).  
*Tinctura cocci.* q. s.  
*Aqua rosæ,* q. s.  
 ad ..... ℥iv (120 c.c.)—M.

The patient boils some water for 10 minutes, allows to cool till tepid,

then adds 1 teaspoonful of the lotion to 3 parts of the water and uses the resulting tepid solution in the eye cup 3 minutes for each eye on the first 2 or 3 days, then for 5 minutes. After a rest of 2 minutes a drop of a solution consisting of 1 minim (0.06 c.c.) of **Trunacek's solution** in water, enough to make 1 dram (4 c.c.) is instilled in each eye. The treatment is carried out by the patient 3 times a day, viz., in the morning, before tea or late dinner, and before retiring. An interval of 1 hour at least should always elapse before the patient goes out. After a week the salines in the lotion are increased to 60 grains (4 Gm.) and the Trunacek's solution to 2 minims (0.12 c.c.), after the second week, to 80 grains (5.3 Gm.) and 3 minims (0.18 c.c.), and later progressively by 20 grain (1.3 Gm.) and 1 minim (0.06 c.c.) amounts, up to 300 grains (20 Gm.) and 14 minims (0.84 c.c.). Some cases show signs of irritation after 200 grains (13.3 Gm.), and the drugs are now changed to **potassium iodide** and **sodium iodide** in the lotion and **iodolysine** injection in the drops, these to be begun in the same strength as the initial preparations of salines and Trunacek's solution, and similarly increased in concentration later. Thereafter, potassium iodide may be combined with sodium acetate, or sodium iodide with **potassium citrate**. Sodium chloride is always added in the lotion. The drops may also be changed to **dionin**. In difficult cases **nux vomica**—tincture—is given internally in doses successively increased up to 4 drams (16 Gm.), and the acetates and citrates of potassium or sodium likewise internally in amounts up to 6 drams (24 Gm.) in 8 ounces (240 c.c.) of solution. The treatment is persisted in for 6 months in most cases and in some for 12 or more months. Anxiety and worry having much to do with the onset of the condition, the word cataract is not mentioned to the patient for some time, or until the opacities have cleared. The results among 100 pri-

vate patients under treatment not less than 3 months were, great visual improvement in 45 per cent., improvement in 41 per cent., stationary cataract in 7 per cent., and no effect in 8 per cent. Recently promising results were obtained in some cases of congenital cataract. W. B. Inglis Pollock (Glasgow Med. Jour., Oct., 1917).

The development of cataract may be retarded by careful and repeated correction of any existing anomaly of refraction and by constant care of the patient's general health. In this connection, it is interesting to note that the present average age of operated-upon cases in this portion of the world (Philadelphia) has gradually lengthened nearly a decade in the past half century.

**Operations.**—At present, there are two operative methods of treating cataract: one by absorption and the other by extraction. The first is applicable to soft cataracts only, and is consequently limited to those cases found in young subjects. It has for its object the bringing of the aqueous humor into contact with the lens fibers by means of an artificial opening made in the anterior capsule of the lens. This is accomplished by entering a needle especially prepared for the purpose through the lower and outer, or preferably the upper and inner, quadrant of the cornea, and incising those portions of the anterior capsule of the lens which are situated opposite the pupillary area.

The pupil should have been primarily dilated as much as possible with some efficient mydriatic. Care should be taken, particularly in very young subjects, that the capsular incisions are not made too extensively, and that they do not penetrate too deeply into the lens structure, in

order that the lens mass may not be disturbed too greatly. For developmental reasons, it is best to wait until the subject is about a year old before any operative procedures are attempted.

General anesthesia is not necessary. The instillation of a few drops of a 2 per cent. strength solution of **hydrochlorate of cocaine** into the conjunctival *cul-de-sac* is sufficient to render the operation painless. The patient should be placed in a recumbent position and the eyelids should be separated either by a speculum or by an elevator and the fingers of an assistant. After the procedure, a few drops of a 1 per cent. strength solution of **sulphate of atropine** should be instilled into the conjunctival *cul-de-sac* and **ice compresses** applied until the eye becomes free from any signs of operative irritation.

If no complications arise and there be sufficient reason, the operation can be repeated as soon as the absorption of the loosened cataractous masses seems to have been sufficiently accomplished and the mass itself has become stationary. The incisions in the second and any subsequent operations may be made more freely, as the danger of swelling of the lens fibers is lessened; this is due to the diminished volume of the lens material. If there is a dense central mass, it had better be removed separately through a peripheral incision while the subject is under the influence of a general anesthetic. If the lens substance escapes as a milky fluid when the capsule is cut it should be immediately evacuated through a small peripherally placed corneal incision. In uncomplicated cases the absorption of the cataractous masses is generally

accomplished in eight or ten weeks' time. In some cases the lens material is so hard that it can be only removed safely and satisfactorily in its entirety, in its capsule, with a hook, loop, or spoon.

The principal complications of the procedure are iritis and secondary glaucoma. The first is supposed to be caused either by pressure or "chemical irritation" exerted by the lens matter on the iris. As a rule, it may be prevented by keeping the pupil well dilated with some powerful iridoplegic or cycloplegic or combination of cycloplegics. If the second form of complication appears, the lens matter should be immediately removed by extraction through a linear incision.

In *traumatic cataract* the patient should be placed in bed as early as possible. **Ice compresses** should be applied either constantly or intermittently to the eye in order to reduce inflammatory reaction, and **atropine** should be instilled at regular intervals to prevent the occurrence of iridic inflammation. Ordinarily, under such a plan of treatment, the lens substance will gradually absorb without any complicating disturbances. The danger of secondary glaucoma with its accompanying symptoms should never be lost sight of, and intraocular tension should be repeatedly tested. If such signs and symptoms should intervene, as much of the lens matter as may be proper at the time should be removed without delay. This may be readily accomplished by a simple incision through the cornea into the anterior chamber, and the softened lens masses carefully and gently coaxed out along the blade of a keratome or the groove of a Daviel spoon.

In operating upon *shrunk cataracts* or membranous opacities, it is not so essential to provoke absorption of the remaining cataractous material as it is to obtain a clear space in the thickened and opaque capsule or remains through which vision can be gotten.

The operation was formerly performed by means of two needles which were passed rather obliquely through the cornea, one near to the nasal and the other close to the temporal border of the membrane. This done, both were pushed backward into the chosen portion of the mass and the points of the instruments separated from one another in such a manner that no traction was exerted upon the iris and ciliary body, thus producing a clear hole in the membrane.

The **De Wecker operation** is the one most generally used, and frequently with good results, although there are inherent elements of danger in it which cannot be eliminated. It necessitates a large corneal opening, thus affording an easy exit for fluid vitreous and a correspondingly easy entrance for infection, in addition to the extensive traumatism to the eye.

The technique of the operation consists in making a 4- or 5- millimeter opening through the cornea with a keratome, and a 2- or 3- millimeter incision in the iris with the same instrument. Through the latter opening the sharp point of a De Wecker scissors is introduced and an oblique cut is made from each end of the iris incision toward the apex of a triangle, forming a converging V. The triangular portion of iris thus formed is grasped with a forceps and removed, leaving a clear central pupil.

But the operation of choice for these conditions, as well as for iridotomy or capsulotomy, is the **Ziegler knife-needle or V-shaped operation**. It possesses all the elements of a perfect operation: ease of execution, safety, and the minimum of traumatism to the eye; and as a consequence, the visual results are superior to those of the older operations. Ziegler, in his exhaustive "History of Iridotomy," has well stated the chief advantages of the knife-needle operation as "ease of incision, the lack of traction on the ciliary body, freedom from post-operative inflammatory reaction, the avoidance of opening an eyeball which may contain fluid vitreous, the lessening of the tendency to iris hemorrhage from lowered tension, and the avoidance of the nebulous scar which often follows a large corneal incision in old inflammatory eyes."

The method of performing the operation is simple: The eye being thoroughly cocainized, a stop speculum is inserted to separate the lids. The eyeball is then grasped with fixation forceps, and the knife-needle is entered on the flat at the corneo-scleral junction, and passed obliquely across the anterior chamber to the lower pupillary margin, when the cutting edge is turned down, and with a quick thrust the point is carried through the membrane. Then with a gentle sawing motion, without pressure, the incision is carried to the upper pupillary margin; the knife-blade is then raised up and carried across to the opposite side of the anterior chamber, where a second puncture is made and the incision carried up to meet the first, thus forming an inverted or converging V.

The second incision must terminate a trifle below the upper extremity of the first, in order that every fiber may be severed and thus allow the flap to fall down behind the lower margin of the iris. At the completion of the operation the knife is withdrawn on the flat.

The requisites for the successful performance of this operation are:—

1. A properly shaped and perfectly sharpened knife-needle. The one illustrated best meets all requirements.



Ziegler knife-needle.

2. All pressure must be absolutely avoided in making the incisions.

3. A gentle sawing motion. In this, and the avoidance of pressure, lies the real secret of success in the operation.

4. Perfect artificial illumination is an absolute necessity, and particularly so in capsulotomies, where the membranes are filmy or web-like in structure.

**Simple linear extraction** is applicable to the removal of both the soft and the membranous varieties of opacity. It is preferred by many operators to discission, and may be employed in any case where the lens substance is sufficiently soft to flow through a small corneal wound.

The operation is performed as follows: After a speculum has been inserted, or the eyelids separated by an assistant, the globe is grasped by a fixation forceps, and the point of a keratome or the tip of a von Graefe knife is entered into the anterior chamber through the cornea, at the limbus. If the former instrument is

used, its tip is passed directly through the corneal membrane, but, as soon as the tip enters the anterior chamber, the cutting blade is laid upon a plane that is parallel to that of the iris. It is then pushed forward until the corneal wound has obtained a length of several millimeters. It is then slowly withdrawn, in order to prevent the aqueous humor from coming away too quickly, with the possibility of a prolapse of the iris. If a von Graefe knife is used, the movements given to the instrument must be very carefully

performed, in order to avoid wounding the iris tissue. The point of a cystotome is then passed into the anterior chamber through the same corneal wound, care also being taken not to injure the iris. Free incision in the anterior capsule of the lens is then made with it. After the incisions have been accomplished, the cystotome is withdrawn and the loosened lens matter is evacuated, as previously explained, by means of a Daviel spoon or a grooved spud. If necessary, the operation may be done with the addition of an iridectomy. In this event, the corneal incision should be slightly longer. After the withdrawal of the knife, the tips of an iris forceps are to be introduced into the anterior chamber and a fold of iris directly over the sphincter of the pupil grasped and gently drawn through the wound and cleanly snipped off with a pair of McClure's or De Wecker's iris scissors. Cystotomy and extraction of the lens massings then follow, as just detailed.

As it frequently happens that lens

matter is left behind, a number of operators practise its removal by suction syringes of special construction. The procedure, however, has never obtained general favor.

The operation for the removal of a hard cataract consists essentially of three steps: the corneal incision of sufficient size to permit of the passage of the lens; an incision, or a series of them, into the anterior capsule of the lens (cystotomy) in order to allow the egress of the lens matter through it, and the delivery of the lens substance from the eyeball itself. Before the actual operation is made, certain preliminary details should be carefully attended to. A general warm bath should be given to the patient the night before the operation. Care should be exercised to make his head clean with Castile soap and water. The bowels should be relieved by a gentle laxative, in order that they may not be disturbed for the first few days after the operative procedure.

The instruments, with the exception of the knives, which should be immersed in alcohol for at least twenty minutes prior to their use, should be boiled. After the cleansing has been completed, they should be kept in a tray of alcohol during the entire operation, being dipped for a few moments in a tray of sterile water just as they are being picked up for use. Care should be taken not to use any differentiating aniline-dye tints for either the immersing or cleansing fluids when they contain bichloride of mercury, as the staining material may injure the corneal epithelium and deeper-lying structures.

The patient having been carefully prepared and the field of operation having been excluded from external

contamination for a couple of hours previously by a few turns of a roller bandage, his eyelids, eyebrows, eyelashes, and adjacent parts should be thoroughly washed with a saturated solution of **boric acid**. The lids should be gently everted and the upper and lower *culs-de-sac* flushed with the same character of solution. Several drops of a 2 per cent. strength solution of **hydrochlorate of cocaine** are then introduced into the eyes at five-minute intervals, for about fifteen minutes before the operation, and a few drops of a 1:5000 solution of **adrenalin** to prevent conjunctival hemorrhage, care being taken that the eyelids are kept closed and that a clean towel is thrown over the field of operation. If possible, the patient should lie flat on his back in the bed that he is to occupy. If circumstances do not permit this, he should be placed upon some form of operating chair or table. The source of light should be situated so that there shall be a field of uniform illumination upon the exact points to be operated upon. If the surgeon be ambidextrous, he may place himself in front of the patient or behind him in accordance with comfort and existing circumstances. A trained assistant should be present and assume such a position that he may be able to hand the instruments to the surgeon or receive them from him with such skill and rapidity that the operator may be able to keep his vision fixed upon the field of operation during the successive stages. Prior to any procedure it is well for the surgeon to speak kindly and quietly to the patient for a few moments to gain his confidence and at the same time inform him of certain movements of the eyes that

may be necessary during the operation. The patient should be cautioned against holding his breath and straining, and told to resist all desire to close his eyes forcibly. By these few injunctions quietly and authoritatively given, the most intractable subjects may be rendered obedient, the soothing words thus given often bearing fruit to the surgeon a hundredfold.

All these minor, but essential, preliminaries being satisfied, the eyelids are to be separated by a stop speculum or a lid elevator held in the hands of a skilled assistant, who is capable, if necessary, of momentarily removing the instrument without any damage to the organ. The patient is asked to look down. The globe is firmly held in any desired position, without any pressure upon it, by gently taking a fold of bulbar conjunctiva about two or three millimeters' distance from the corneal limbus within the grasp of a fixation forceps held with one hand, while with the other the corneal section is to be made. The knife most generally employed is one introduced by von Graefe, which consists of a long, straight, narrow blade converging at its far extremity into a sharp point. Unless contraindicated, the primary puncture should be made in the limbus at the outer extremity of a horizontal line, which, as a rule, would pass three millimeters below the summit of the membrane. The cutting edge of the knife should be situated upward and its point directed toward the center of the cornea. After the tip of the knife has been made to enter the anterior chamber, it should be carried directly across and re-entered into the limbus at the point desired. The section should

then be completed by an upward movement so regulated that the section is kept true and smooth throughout its entire extent. The first stage of the operation being completed, the surgeon next addresses himself to the performance of the second stage, or that of **capsulotomy**, or so-called **cystotomy**. Directing the patient to look down and without any fixation instrument in position, if possible, he introduces a cystotome, with the heel of the cutting point first, between the lips of the corneal wound, and inserts the point of the instrument into the anterior capsule, without dislocating the lens, in such a manner as to be able to make a series of as free incisions as he may believe desirable, and in such positions as he may deem the best. These having been obtained, the cystotome is withdrawn in such a way that the iris is not wounded during the procedure. The avenue of escape for the lens having been made, it remains to practically complete the operation by the performance of the third stage, or that of the delivery of the lens. The surgeon should, with a Daviel spoon upon the sclera just below the lower edge of the cornea, and a spatula held in the other hand and placed upon the sclera just above the corneal section, make a series of delicate, yet steady, upward and forward pressures and counterpressures until just one-half of the lens has engaged in the corneal wound, when, by a dextrous and slightly tilting and upward motion from side to side, the lens will emerge without any complication whatever, and the corneal flap will fall smoothly into place. Should the pupil not be round and should any lens *débris* be seen, the eyelids are to be closed and a slight

gentle rotary motion made upon the globe through the upper lid by the fingers. If there be any cortex remnants, the stump of the flap is to be slightly depressed and the masses gently, though as completely as possible, washed out of the anterior and posterior chambers by free irrigation from varying positions with warm sterile water or **boric acid solution**, without the introduction of any instrument whatsoever into the chambers.

After the lens has been delivered and anything, such as blood-clots and lens *débris*, which might prevent the proper union of the lips of the corneal wound has been removed, the conjunctival *cul-de-sac* is to be flushed with a warmed **solution of boric acid**, and the pupil and corneal flap seen to be in proper positions. The eyelids of both eyes are then gently closed and held together, if necessary, by one or two narrow strips of isinglass plaster. No pressure should be made upon the eyeball.

A few carefully adjusted and smoothly applied turns of gauze bandage over squares of sterilized gauze properly covered by pledgets of absorbent cotton should be made without disturbing the patient. Strict injunction to remain quiet for at least twenty-four hours' time should be given, any necessary desires being properly cared for by competent attendants.

If no pain be complained of, the dressings should be allowed to remain for twenty-four hours, at the end of which time they should be removed, the eye inspected, and the conjunctival *cul-de-sac* gently flushed with a warm solution of **boric acid**. If all has gone well it will be found

that the anterior chamber has re-established itself and that the eye is quiet. If there be any injection, if the pupil is small, or if any sign of inflammatory reaction be present, a drop or two of **sulphate of atropine** or, better, **hydrochlorate of scopolamine** should be instilled. At the end of forty-eight hours' time the dressing over the sound eye may be removed, but that on the operated eye, which can be made lighter, should be allowed to remain for at least another day, when plain smoked glasses or, if unobtainable, a suitable shade can be worn.

To prevent any tendency to prolapse of the iris and to favor smooth healing of the corneal incision, it is essential that the patient should rest absolutely quiet in bed for the first forty-eight hours. If he be old and feeble, more latitude can be given to his movements, which must be accomplished by the aid of careful attendants. At the end of the second day, a bed-rest may be employed, and on the third day, if the healing has been uncomplicated (which under the circumstances will be so almost without exception), the patient may be allowed to sit up. For the first twenty-four to forty-eight hours the **diet**, which is to be regularly given, should be liquid and semisolid. On the third day the bowels can be opened by a gentle laxative. After this, liberal nourishment may be ordered.

The operation which has just been described is what is known as **simple extraction**, or extraction without iridectomy, and should be the one chosen in all suitable cases in which there are no contraindications.

Many operators, however, still



make use of an **iridectomy** before they expel the lens, justly claiming for this method that it enables them to get rid of any remaining cortical matter much more readily. They also state that it prevents prolapse of the iris and that the lens may be extruded through a smaller wound. The sole difference in the procedure consists in removing a wedge-shaped piece of iris tissue after the corneal section has been made. To do this the tips of a pair of iris forceps are introduced so as to reach the sphincter pupillæ. The inclosed iris tissue is gently grasped at the pupillary border and steadily withdrawn through the center of the wound. The extended portion is excised by a single clip made with an iris scissors. The free edges of the coloboma then made are smoothly set into position by an applicator or a flat spatula.

Those who prefer extraction without iridectomy urge that the advantages of a round, mobile pupil make it the operation of choice. The contraindications are: an unripe cataract; increased intraocular tension; a small, rigid pupil, and an intractable patient.

Despite the most careful precautions, prolapse of the iris does occur in a few cases of simple extraction, usually appearing during the first twenty-four or forty-eight hours. If it be small, it may be let alone. If it be considerable, and the lips of the wound remain ununited, the line of corneal incision may be opened and the prolapsed portion of the iris excised with an iridectomy scissors. Should the prolapse occur after the wound has united, it is best either to wait until about the tenth day, when a formal iridectomy can be made, or, if not productive of any irritation and

the pupil is not much distorted, it can remain undisturbed, cicatrization and flattening subsequently taking place.

To prevent prolapse of the iris, numerous modifications of the classical operation for cataract have been devised, the most effective being the Kalt corneal suture, the Van Lint sliding conjunctival flap, and the Hess peripheral iridectomy.

While each of these modifications possesses well-known merits and is applicable to certain cases, yet not one of them has come into general use. The Van Lint operation is well worthy of consideration. The method of performing it is as follows: The conjunctiva is dissected along the corneal limbus from the horizontal meridian upward, the dissection being carried 8 or 10 mm. above the superior margin of the cornea. Two fine-silk sutures are then inserted into the conjunctiva, one on each side of the cornea.

The needles are introduced beneath the conjunctiva, the inferior one about 2 mm. below the horizontal meridian and the superior carried sufficiently high to bring the conjunctiva down over the upper one-fourth of the cornea. After the introduction of the threads, the operation is done in the usual way, and when completed the threads are tied and cut close to the knots, in order not to irritate the cornea.

A drop of eserine is then instilled and a binocular bandage applied and allowed to remain for forty-eight hours, at which time the anterior chamber is usually re-formed, and atropine may then be instilled.

The stitches are allowed to remain for five or six days. The conjunctiva retracts by degrees, requiring from

forty-eight hours to five or six days to clear the cornea.

The advantages of the operation are: ease of execution, protection against prolapse of the iris and infection, and coaptation of the lips of the wound, the conjunctiva acting as a splint.

The procedure in the **Hess operation** is as follows: The corneal incision is made in the usual manner, after which the corneal flap is grasped with a forceps and turned back, exposing the iris, which is incised close to the scleral margin of the wound with the sharp point of a De Wecker scissors. The incision should be parallel to the cornea and about 1 mm. in length. The operation is then completed in the usual manner, and a few drops of eserine instilled. The buttonhole in the iris prevents the aqueous which collects behind it from forcing it forward into the corneal wound.

The latest statistics of this operation show less than 0.7 per cent. of iris prolapses.

In certain cases in which complications are feared, or when it is advisable to hasten the maturity of the cataract, an iridectomy known as **preliminary iridectomy** can be performed some time before the extraction of the lens is made. If it is desired to ripen the lens after the iridectomy has been performed, the lens may be triturated with a spatula either directly applied to the anterior capsule or indirectly through the cornea. Rapid swelling and opacification of the lens are said to follow these procedures, and the extraction in many cases is made possible in several weeks' time after the operation. The lens substance, however, in these cases seems to have obtained

an undue degree of friability, which may be detrimental to its complete removal. In this class of cases it is much better to remove the lens in its capsule. Many surgeons assert that simple extraction with the section made as much as possible in the avascular cornea gives the best results in "black cataract."

Removal of the lens in its capsule, as is practised in some countries, is a preferred and invaluable plan of procedure in the hands of expert operators.

Some operators have adopted the method of syringing the anterior chamber after the removal of the main body of the lens, in order to remove any remaining cortical matter. Although this plan entails the bringing of another instrument, which may be an additional source of infection, into the eyeball, and is always attended by more or less local reaction, its advantages, according to some surgeons, seem to be so many that its employment has become more general with them.

Many of the accidents occurring during cataract extraction are the results of want of skill. Loss of vitreous humor should be guarded against, as sooner or later such an accident is harmful to the integrity of the eye. It can be often prevented by the employment of fine sutures placed in the cornea. Should the sclera collapse during the procedure, the lens may be safely removed within its capsule by the use of a wire loop. Propulsive hemorrhage is, fortunately, a rare complication. It is almost always ruinous to the eye. It is met by local and general methods that are best adapted to each individual case. In some instances, however, it han-

pens that the patient's condition is such that a successful result can scarcely be expected. Deafness, loss of self-control, and great stupidity are all harmful and even injurious at times.

Case of hemorrhage in the anterior chamber four days after cataract extraction. The anterior chamber was almost filled with blood; there were repeated hemorrhages. The urine and blood-pressure tests were negative. The hemorrhage gradually cleared up. W. H. Wilder (Jour. of Ophthal. and Otolaryn., May, 1908).

Although planned with the utmost exactness, it sometimes happens that the size of the lens is misjudged and the normal corneal section is made too small. If this occurs, the incision should be enlarged by one or two clean snips with a pair of scissors. Should prolapse of the vitreous humor take place during the delivery of the lens, an iridectomy had better be carefully done and the lens removed with a loop or a spoon. Prolapse of the vitreous humor occurring after the extraction of the lens is much less serious for the time being. It interferes, however, with the proper coaptation of the lips of the wound and renders inflammatory action more liable, while in many cases it becomes a most harmful complication for the future welfare of the organ.

Loss of vitreous, irrespective of the amount, adds to the danger of primary infection, but much depends on the care taken in preparing the field of operation; the danger of the occurrence of iridocyclitis during the stage of healing is materially increased by the loss. The increased activity of the blood-vessels and lymphatics during repair excites changes in the iris and ciliary body, ending in a hyalitis, with closing of the pupillary space and anterior phthisis.

When the vitreous is once lost, what takes its place is probably aqueous; the framework is never replaced and the vitreous becomes fluid throughout. Floating particles increase, fibrillary bands are thrown out to take the place of the normal reticulum, and, these contracting, cause minus tension and retinal detachments, followed by the characteristic square atrophied globe due to the action of the recti muscles on the softened globe. J. M. Ray (Jour. Amer. Med. Assoc., July 6, 1907).

Usually there is some discomfort for several hours after the operation. Should this continue and be at all marked, the bandage should be removed and the eye inspected. At times great relief will be given by gently pulling down the lower eyelid and giving exit to an accumulation of tears, or by allowing a faultily placed eyelash or lid border to fall into proper position. If the eyeball appears the least injected and the slightest signs of iritis be present, atropine should be immediately instilled into the conjunctival *cul-de-sac*. If suppuration appears, it usually takes place before the third or fourth day, and is traceable to infection, generally from lachrymal disease: in a few instances it is dependent upon a lack of nutrition to the eye. If it is due to the former, it is best combated by cauterization of the edges of the incision, the instillation of sulphate of atropine, and the use of hot compresses. The latter form is best cared for by attention paid to the general health.

Infection after cataract extraction, in spite of all known methods of asepsis, has not been altogether overcome. Statistics from operators of large experience still show that this accident occurs in from 1 to 4 per cent.; Graefe himself had reduced it

to 5 per cent. years ago, before asepsis was heard of.

After infection has occurred, while the outlook is bad, it is not hopeless. Local treatment consists in cauterization of the wound, subconjunctival injections, and germicides inserted or injected into the anterior chamber. The cauterization is accomplished by means of the **galvanocautery, silver nitrate, mercuric bichloride, carbolic acid, and the thermocautery.** Darier declares that the last should not be used. He is the special advocate of subconjunctival injections, the value of which, however, still remains to be determined. The insertion of **iodoform** in rods or disks containing up to 70 per cent. of the remedy is unquestionably of service if introduced early enough, the earlier the better. The injection of other substances than iodoform has received little attention, though **bichloride, 1:1000,** has given good results. The writer reports a strikingly satisfactory case where this method was employed with the saving of useful vision. In all cases the general treatment should be stimulating and supporting. Hansell (*Annals of Ophthal.*, April, 1905).

Case of infection following cataract extraction treated by **vaccines,** with rapid recovery. The patient was a Filipina of the lower class and the time of operation May, 1908. The operation itself was uneventful and the wound closed promptly without any prolapse of iris, but on the third day symptoms of infection developed and on the fourth pus was exuding through the wound. A culture was obtained from the pus and a vaccine prepared. The first injection was given seven days after the operation, subconjunctivally. The eye continued to grow worse. Two days later a second injection was given intramuscularly in the arm. Improvement was rapid, the eye being noticeably better the next morning. R. P. O'Connor (*Ophthalmology*, April, 1911).

For monolateral cataract up to middle life, **discission** is to be con-

sidered as a proper procedure; and in many cases the patient will prefer it to extraction. The first discission should make only a short opening in the capsule; but may well penetrate to the center of the nucleus, so that disintegration of the latter may begin as soon as possible. The amount of swelling from a given interference will be proportioned to the size of the opening in the capsule, and the absence of previous change in the lens substance. Severe reactions and surgical shock are provoked by the presence of large masses of lens substance in the anterior chamber. Possible hemorrhage from making puncture through the vascular limbus, causes no danger to offset the greater safety from infection secured by this point of entrance. Edward Jackson (*Jour. Amer. Med. Assoc.*, July 29, 1916).

Both eyes should not be operated upon at one sitting, any unforeseen and harmful local and systemic complications arising after the primary procedure being given opportunity for avoidance after the second operation. Several weeks' interval at least should be allowed to elapse between the two extractions, even when the cataracts are about equally mature.

An eye whose lens has been removed is termed aphakic, and, in order that its vision may be useful, it must be provided with an artificial lens corresponding in relative strength to the crystalline lens that has been removed, plus a cylindrical one to correct any astigmatism resulting from cicatrization of the corneal incision. To this artificial lens must be added a convex spherical one of two or three diopters' strength for use during near work. As cicatrization is usually not completed until four to six weeks after the operation, it is better to postpone ordering glasses until at least that time.

No case can be considered as having been successfully operated upon until at least three to six months after the actual procedure.

The old method of depression and reclination (couching) has, by reason of coarse and destructive after-results, been practically abandoned, except in a few appropriate cases among the old and decrepit, where, for example, sight is legally required for a brief period of time.

Secondary or membranous cataract is an opacity either of the posterior or anterior capsule, which develops after the extraction of the lens. The capsule, owing to the proliferation of the epithelial cells on its under surface, becomes thickened, and thus greatly reduces vision.

In order to relieve this condition and restore vision, it becomes necessary to do a second operation,—**capsulotomy**. This should be postponed for some weeks, until the eye becomes perfectly quiet. The operation is best performed by the method already described.

Erythropsia, or colored vision from changes in color perception, is said by some to be the result of after-image dazzling. It may follow both the simple and the combined forms of extraction, especially the latter, even several years after the procedure. It is quite common in some countries, particularly in India.

The writer has operated on several patients over 80, and reports here a case in which the patient was over 95, approaching 96. He was in good condition for his age, and this is the main criterion as to operability. Santos Fernandez (*Revista de Med.*, y *Cir.*, Feb. 25, 1918).

A method which is gaining favor with American surgeons is Major H.

**Smith's operation.** Its purpose is to extract the capsule completely (a procedure first performed by the Pagenstechers, though attempts to do so had previously been made by Daviel), thus leaving none of the lens matter, which often gives rise to more or less severe complications and occasionally to disastrous consequences.

The writer is now of the opinion that the combination of lens capsule in the wound and the liquefying *débris* of lens matter in the aqueous chamber are of the nature of a chemical irritant, causing iritis and iridocyclitis, and also interfere with the normal healing of the wound, and that these factors taken together account for the fact that in India the capsulotomy operation is followed by an incomparably greater mortality of eyes from all causes than is the case with the intracapsular operation.

A beginner should do an iridectomy. The incision should be large; most of the failures in the novice are due to non-observance of this rule.

In the case of an immature lens or of a hard cataract, with a spatula in the operator's left hand ready for use if required, he proceeds to press back with the point of a strabismus hook toward the optic nerve; the point of the hook being placed over the lower third of the lens, the pressure is steady and the point of the hook should not be moved until the upper edge of the lens tilts forward and is thus seen to be dislocated, having been made to swing on its transverse axis. The moment the lens at the wound is seen to be dislocated, the pressure through the point of the hook is gradually turned more and more toward the wound, pressure being maintained all the time so as to keep the lens up to the sclerotic margin of the wound, the pressure with the hook becoming gradually lighter and lighter and the hook gradually sliding after the lens until the cornea is folded beneath it; at this stage it is delivered. In a low-tension eye

the beginner should follow up the lens with the spatula in addition to the hooks, as with it he can maintain a sufficient tension in the eye and thus allow his right-hand instrument to follow up the lens more lightly.

In the case of intumescent lenses and Morgagnian cataracts pressure is made on the lower border of the lens and traction is made from this point in the direction of the patient's feet, by which almost invariably these lenses are made to dislocate below at first and to turn a half-somersault. This pressure and traction are over the zonule. As soon as the lens turns up into the wound, showing that it is freely dislocated below, the operator should cease to make traction toward the patient's feet and make direct pressure first backward, then backward and upward, and finally more and more toward the wound, folding the cornea beneath the lens until it falls over on the outside of the cornea.

The hypermature cataract is the most difficult to dislocate. To remove this type of cataract the spatula is dropped behind the lens the instant the edge of it is seen at the wound, keeping the back of the spatula throughout against the sclerotic margin of the wound. The lens is pressed against the spatula from the outside and thus made to slide up along the inclined plane of the spatula.

Careful reposition of the iris is very important and prevents complications. Vitreous should be snipped off with scissors if it escapes, and not left in the wound to act as a drain. The writer is opposed to the various devices used for dislocating the lens with an instrument inserted into the interior of the eye. Major H. Smith (*Ophthalmic Record*, Feb., 1910).

The technique of the operation is not complicated, but it requires dexterity and in a measure special training. As stated by G. T. Birdwood (*Indian Med. Gaz.*, Jan., 1910), it is an operation that allows of few mis-

takes; a misplaced incision, either too small or too far back, or undue or misapplied pressure will end in its failure. It requires persistent steadiness of hand. The same writer describes the operation as follows:—

The operator must sit on a stool two feet high behind the patient's head. The patient is on a table two feet seven inches high. This is important, as it gives the operator great steadiness of hand compared with that obtainable in the standing position. The eyebrows, lids, and instruments are sterilized in whatever methods each operator prefers. The speculum is inserted between the lids. The eyebrow is then strongly drawn upward and the speculum also raised off the globe. A stream of 1 in 2000 perchloride of mercury is then strongly douched into the fornices from an irrigator three feet above the patient's head. By drawing the eyebrow upward every corner of the upper fornix is made visible and easily reached by the lotion.

The incision is then made. It must be large. It is very nearly but not quite half the circumference of the cornea. It is commenced slightly behind the sclerocorneal junction, and brought out slightly in the cornea, the edge of the knife being turned slightly upward before completion of the incision.

An iridectomy of moderate size is then done. The speculum is removed and all fluid is squeezed out of the conjunctival sac by pressing a piece of cotton-wool across the closed lids from the inner to the outer canthus. The assistant then takes a stout strabismus hook in the thumb and index finger of his right hand and draws the upper lid vertically forward. The

operator then cannot see the globe unless he leans over the right shoulder of the patient. At the same time with the middle, ring, and small finger of the same hand the assistant draws the eyebrow forcibly up. In this way there is no pressure whatever on the globe. With the thumb of his left hand he draws the lower lid down. Smith attaches great importance to the method in which the assistant elevates the lid. It is a little difficult at first, but after a few days an intelligent assistant can be taught it. The operator then leans well over the right shoulder of the patient and looks at the globe over the cheek. He takes a strabismus hook in his right hand and places the point on the cornea over the point where he thinks the lower edge of the lens is. Pressure is made at first downward, and then from side to side and backward and forward, keeping up the downward pressure gently till the edge of the lens appears in the gaping wound. The spoon, sometimes held in the left hand, is placed on the cornea beside the hook and used to steady the lens and keep up the tension at one side, while the point of the hook increases the tension at the other side; as the lens emerges, the point of the hook follows it up. Often the hook alone is sufficient to expel the lens. Sometimes, by drawing the point of the hook toward the feet, the corneal incision is made to gape and corneal flaps can be drawn over the lens like a foreskin over the prepuce. Sometimes the lower corneal flap can be drawn downward by the point of the hook, and then gently pressed under the lower edge of the lens as it is emerging, so that the lens emerges lower end first. These cases Major

Smith calls "tumblers," as the lens tumbles out lower end first.

As the lens emerges from its bed the hook is turned on the flat, and either the point of the hook or the bend of the hook is gently used in the final separation of the lens from the hyaline membrane; sometimes the lower corneal flap seems to be used as a medium to express the lens from its bed; after removal of the lens the cornea sinks down into a hollow and a pair of iris forceps or a strabismus hook is used to adjust the pillars of the iris and the edges of the incision. The eye is then closed and dressed.

The essential points seem to be:—

1. That the operator should be sitting down to get the necessary steadiness of position.
2. The incision should be very large.
3. An iridectomy should be done.
4. All pressure must be lifted off the globe by elevation of the upper lid forward and retraction of the eyebrow by a trained assistant in a special manner.
5. The operator must appreciate and understand the effect of the pressure of the hook on the lower edge of the lens, and the relation of the lens to its bed and to the lower corneal flap. He must be quick to see the effect of drawing the lower flap toward the feet, or the possibility of pushing the flap under the lens.

If the capsule should rupture when the lens is half-way out, it is best to take a wide-pointed dissecting forceps, and catch the lens and capsule in them, and remove both if possible together.

A preliminary capsulotomy, especially in immature and hypermature cataracts, is indicated only in such cases as one would choose for the simple extraction; where, however, a preliminary iridectomy is indicated,

the capsulotomy should be made in advance of the extraction. The writer employs a specially devised capsulotomy knife resembling a miniature scalpel, with a cutting surface 2 mm. long, and does the capsulotomy the day preceding the extraction of the lens. **Homatropine** is used to dilate the pupil for the first operation. The writer mentions the following advantages of the preliminary capsulotomy: (1) The capsulotomy knife can be made superlatively sharp and efficiently cuts the capsule in both directions. (2) Ample space is given through the dilated pupil, and the point of the knife may be kept fully in view during the division of the capsule and, furthermore, the operator has the satisfaction of knowing that this is perfectly performed. (3) Only through the grossest carelessness can the suspensory ligament be ruptured or the lens dislocated, for it is held firmly in place by the pressure of the vitreous behind and the aqueous in front. (4) The iris cannot be wounded or entangled in the instrument, and there can be no bleeding to obscure the view of the operative field. H. E. Smith (*Arch. Ophthal.*, Jan., 1912).

Patients who have reached the age of 90 or over should be handled with very great care, surgically and otherwise; the following precautions are recommended before operating: a very careful examination of the eye and of the conjunctival sac; most thorough physical examination, including the mental condition, a stay of two weeks in an institution for this purpose being none too long; a preliminary iridectomy; strict asepsis. After operation the patient must be kept upright as much as possible, and quiet, but cheerful and hopeful. The eye not operated upon should not be bandaged. Answers to letters sent to about 300 oculists, asking for their experience along this line showed that wounds in the very aged heal as well as in persons of younger years. If the very aged parent is in good health physically and mentally,

a cataract operation should not be denied him. G. F. Keiper (*Amer. Jour. of Ophthal.*, Nov., 1911).

The advantage to be obtained by Major Smith's procedure is the avoidance of secondary cataract, for, after the lens and its capsule have been removed, there is nothing left to block the pupil, and the rays of light pass into the interior of the eye without interruption.

From the observation of some cases operated on in Philadelphia by the **Smith method**, and from a study of the statistics, as well as from the testimony of others who have performed the operation, the writer is convinced that the operation is much more difficult than that performed with capsulotomy, and that it is invariably attended with much greater loss of vitreous. As a consequence of the greater danger of loss to which it exposes the eye, he is therefore decidedly of the opinion that the practice of the removal of the lens in its capsule should be reserved for hypermature cataracts.

From an experience gained by operating upon more than 600 cases of senile cataract, the writer believes that the best results are to be obtained only by the greatest conservatism and by the exercise of the most sedulous care in carrying out all the details of a careful removal of the lens by **capsulotomy**. W. C. Posey (*Amer. Jour. of Surg.*, Dec., 1909; *Jour. of Ophthal. and Otolaryn.*, March, 1910).

The writer has performed the **Smith operation** a number of times and has never had a prolapse of the vitreous when the patient did not look downward during the manipulation, or immediately subsequent to the operation, before the eye was closed. Myles Standish (*Ophthal. Record*, Sept., 1911).

To insure even pressure over the eyeball, the writer uses swabs of wet sterilized wool applied as follows: The wool is pulled, not cut, into pads, about 1 inch thick and 3 inches in diameter. The pads are then steril-



ized by boiling in 1:5000 biniodide solution. After the completion of the operation 2 of these, sopping wet, not wrung out, are laid on both eyes. They are gently pressed down over the eyes, so that the swab becomes molded to the eye and fills in the hollows round it. Over this swab is placed a wet pad consisting of lint or 6 layers of gauze and then a figure-of-8 bandage is applied fairly firmly. On opening the dressing next day the wool gauze will be found dry and forming a complete mold of the eyeball and orbital opening. This wet molding method is very comfortable and produces no feeling of uneven pressure while it allows the eye to move easily, though keeping the eyelids closed. Maynard (*Indian Med. Gaz.*, Apr., 1916).

In the opinion of the writer the **Barraquer method** is the most important step in ocular surgery. With other technique more or less of the lens and parts of the capsule are left behind, entailing complications. Barraquer regards the cataract as a cyst with degenerated contents, which explains the virulence of post-operative iritis, and emphasizes the necessity for removing all the contents and the enclosing capsule. With the Smith forcible technique there is liable to be loss of vitreous. This is avoided with the Barraquer method, as pressure does not have to be applied. Iridectomy is rarely needed with it. The operation is reduced to the incision of the corneconjunctival flap. After this the lens is drawn out by suction with a special kind of cupping glass which fits over the anterior surface of the crystalline lens, through the pupil, without the slightest injury of the iris. The cataract comes out with it when the instrument is gently withdrawn. All other methods expose to the danger of hernia of the vitreous; Barraquer's method eliminates this danger. He has applied it to date in 127 cases of all kinds of cataract and has never had any operative mishaps with it. He prophesies that this new Spanish

method will supersede Smith's Indian method. Wieden (*Siglo Medico*, July 21, 1917).

The **Barraquer method** of extraction of cataract in the capsule by suction is criticised by the writer. He thinks that in the majority of cases those methods are to be preferred in which the capsule is not extracted. However, he deems the Barraquer method especially useful in luxation cataracts, those accompanied by a foreign body, the capsulolenticular, and the incomplete. Corneal suture is an excellent complement in all such cases since it prevents the loss of vitreous, which is the principal defect of extractions *in toto*. Marquez (*Rev. de med. y cir. pract.*, xli, 219, 1917).

Barraquer, of Barcelona, now has a record of 630 cases of cataract which he has removed in the capsule by his method of **vacuum aspiration**. Simple extraction was done in 391 cases, the combined extraction in 289; with a conjunctival flap in 436 and with a suture in 194. Vision was left from 0.7 to 1 in 398; from 0.3 to 0.6 in 185; from 0.1 to 0.3 in 44, and 0 in 8. In the total 630 cases, 34 complications were encountered, hernia of the vitreous in 5; inversion of the flap in 2; rupture of the capsule in 3; luxation of the lens in 2; infection in 2; hernia of the iris in 5; hemorrhage in the anterior chamber in 3; impaction of the zonula in 4; hyphemia in 7. Moerno (*Siglo Medico*, Jan. 4, 1919).

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**CATECHU.** See GAMBIR.

**CEREBRAL ABSCESS.—DEFINITION.**—Cerebral abscess is a focal suppurative encephalitis affecting either the gray or white matter or both. The abscess may be single or there may be several separate foci of suppuration. (See, also, ENCEPHALITIS.)

**SYMPTOMS.**—The symptoms may be of acute rapid onset or they may develop slowly and insidiously during several weeks or even months. Clinically the symptoms are divisible into those which are general and those which are local or focal, the former being those of general diffused cerebral compression or irritation, the latter representing perversion or interruption of motor, sensory, or special function, varying according to the anatomical site of the abscess. Among the general symptoms which are most common are headache and lassitude, perversion of the intelligence and the emotions, disturbances of sleep and of consciousness, vertigo, vomiting, convulsions, and sometimes optic neuritis. These general symptoms will vary somewhat in degree and character, according to the mode of onset. When the abscess produces symptoms rapidly the headache is more intense; as a rule, there is a more active or decided involvement of intelligence and consciousness, sometimes manifesting itself in acute delirium or in profound somnolence or semicomatose; there may be rigors, with an abrupt and decided rise of temperature, and the whole picture suggests an active meningitis, from which, indeed, it may be, and often is, difficult to distinguish it. General convulsions are not uncommon in cases with acute onset. Optic neuritis is a symptom varying in frequency with different observers. By some it is considered comparatively infrequent; by others quite common. Okada, a Japanese physician, reports optic neuritis as present in more than 50 cases in a series of 88. When the symptoms are of slow, gradual development they are usually much less intense in degree. The headache is relatively mild; the

vertigo may be slight; vomiting may be absent or occur only rarely; instead of somnolence or coma there may be simple apathy, and a state of simple mental confusion with irritability may appear instead of delirium. The temperature in such cases is usually normal or subnormal; occasionally these patients will exhibit periods of remission attended with a very dangerous semblance of well-being and comfort. Sooner or later the disease becomes aggressive, and evidences of focal disturbance may be observed by which the site of the abscess may be determined. These focal symptoms will vary, as has been stated, in accordance with the function of the brain area affected by the abscess. There are several methods of approach—short-cuts, so to speak—to a consideration of the focal symptoms. Brain abscess is apt to develop in certain areas according to the cause with a constancy which is of decided value in localization. When due to an extension from ear disease, for example, the abscess is nearly always found in one of three localities: the temporosphenoidal lobes; the cerebellum, or the pons-medulla region. More than three-fourths of all cases are located in the temporosphenoidal lobes or the cerebellum. If the pus enters through the medium of a secondary phlebitis of the lateral sinus the abscess will quite probably be found in the cerebellum.

In an analysis of 100 cases of cerebral abscess, with special reference to symptomatology, the writer noted that most of these cases have followed chronic middle-ear suppuration. The route of infection was through the tegmen tympani in 40; secondary to epidural abscess in 6; secondary to sinus thrombosis in 6; in 6 cases through the mastoid antrum; secondary to infection through

the squama in 2 cases, while in 9 no bone defect was found. One case was secondary to a cerebellar abscess.

Headache and vomiting and slow pulse were prominent symptoms, as was vertigo; later coma and stupor, a little dullness, and aphasia. Mental dullness and optic neuritis were frequently observed. Aphasia was noted in 10 cases, nystagmus in 4, paretic symptoms in 17. In 15 they were on the side opposite the brain lesion, in 2 on the same side. Dench (*Amer. Jour. of Med. Sci.*, Nov., 1907).

In cerebellar abscess and acute suppurative labyrinthitis there are three chief tests on the labyrinth by which the nystagmus is brought about, the caloric, the rotary, and the galvanic. The caloric is the most valuable. Given a case of strong rotary nystagmus to the right, the right ear being diseased, and the patient is lying on his back. Sterilized water at 21° C. is allowed to flow in through the external meatus. If after a lapse of from twelve to sixty seconds we do not get a nystagmus to the left and the nystagmus to the right is not lessened, this nystagmus to the right must be due to some intracranial condition. The absence of the right caloric reaction shows that the right canals must be already destroyed, and that they are no longer capable of sending impulses, and again, if all this spontaneous nystagmus were due to the destruction of the right canals, it would be to the left and not to the right, and thus we can settle the point that the nystagmus is not due to any labyrinthine condition. But should the patient have rotary nystagmus to the left and not to the right, we can again apply the caloric test, but in this case the water must be at a temperature of 39° C., since we wish, if possible, to create a nystagmus to the right. If we find the function of the labyrinth remains, even though it is impaired to some extent, we must diagnose suppuration of the

labyrinth and not cerebellar abscess, but should this spontaneous nystagmus not become less after four or five days we must diagnose cerebellar abscess in addition. Should the patient have a strong rotary nystagmus to the right or left, and if on application of the caloric test the right canals are found capable of being irritated and if this nystagmus does not get less as time goes on, then it is evident that the case must be intracranial. J. Harper (*Lancet*, May 7, 1910).

If the pus enters the superior petrosal sinus it will be found in the cerebrum and probably in the temporal lobe. When caused by trauma the abscess usually bears some relation in its location to the site of the trauma, though sometimes the pus formation is at a remote part of the brain from the seat of injury, as, for example, in the occipital lobe, the blow having been received over the frontal region.

The spread of infection from the ear to the brain is accomplished in four ways: (a) Through the tegmen tympani into the middle fossæ. (b) Through the internal auditory meatus and aqueducts into the posterior fossa. (c) Through the inner table covering the sigmoid groove which covers the sinus, into the posterior fossa. (d) Through the spread of the infection from one fossa into the next. The extension is sometimes direct, and sometimes through the occurrence of phlebitis. All varieties of brain abscess are of infectious origin. They may be the result of infection of the pharynx of the nasal fossæ, and air sinuses, or, as in the great majority of cases, the result of aural infection. W. Sohler Bryant (*Amer. Jour. of Surg.*, Sept., 1909).

The writer gives the following points in the diagnosis of tumor or abscess in temporosphenoidal lobes: The symptom-complex of tumor in the right temporosphenoidal lobe in a right-handed person is as follows:

Epileptiform convulsions, dreamy states, crude subjective sensations of smell or taste, with or without involuntary reflex movements of mastication. Subsequent to major attacks: in most cases transient weakness of the left lower facial muscles, usually most evident on emotional expression; less often the left arm and leg temporarily paretic; left abdominal reflexes diminished or absent, deep, increased; the left plantar reflex may be of extensor and the right of flexor type. Bilateral papilledema usually of greater intensity on the right side. Reflex change and motor symptoms on the left side, at first merely postepileptic, but later become persistent phenomena. No word-forgetfulness after major attacks or at other times. No speech defect. The symptom-complex of tumor in the left temporosphenoidal lobe in a right-handed person is as follows: Difficulty in naming objects seen and recognized; later, word-forgetfulness in conversation; later, in-apposite words and phrases, with instant recognition of mistake when made, but inability to prevent perseveration of verbal errors. Reading aloud and writing to dictation are well performed; spontaneous writing is poor. Epileptiform convulsions of varying severity and frequency; dreamy states or analogous pathological psychic conditions; crude subjective sensations of smell or taste, with or without involuntary reflex movements of mastication. Subsequent to major attacks: in most cases transient weakness of the right lower facial muscles, usually most evident on emotional expression; less often the right arm and leg temporarily paretic; right abdominal reflexes diminished or absent; deep, increased; the right plantar reflex may be of extensor and the left of flexor type. Bilateral papilledema, usually of greater intensity on the left side. Reflex change and motor symptoms on the right side at first are merely postepileptic, but later become persistent phenomena. The existence

of hemianopsia would, of course, indicate precisely the side of the lesion. F. Kennedy (Jour. Amer. Med. Assoc., June 3, 1911).

The writer supports the position taken by Koerner, in 1894, that otogenous abscesses in the temporal lobes frequently affect the oculomotorius; that the paresis is almost always partial, affecting first, or alone, the fibers that supply the levator palpebræ and sphincter iridis, and that these pareses are not nuclear, but are due to an injury of the nerve trunk. This is in opposition to the view recently advanced, that such lesions must produce total paralysis of the nerve, and that partial pareses are nuclear. F. Brandenburg (Beiträge z. Augenheilkunde, June, 1912).

The absence of ocular symptoms does not justify the exclusion of intracranial involvement complicating aural disease, but when considered in conjunction with other symptoms it is a valuable guide to a timely operation. Choked disc and optic neuritis are the earliest and most important evidences of intracranial involvement. Jobson (Laryngoscope, xxv, 7, 1915).

Cerebral abscess, when due to necrosis or disease of the bones of the face, is frequently located in the frontal lobes or at the base; when from syphilis or tuberculosis, its site is, as a rule, the motor convexity, the base, or the cerebellum. Pyemia and other constitutional infections are apt to induce multiple abscesses, which seem rather prone to develop in the distribution of the middle cerebral artery of the left hemisphere. The data of cerebral localization should be applied in determining the site of the abscess in each instance. The principles of localization in cases of uncomplicated brain abscess located in active regions apply with unusual constancy, the diffusion of symptoms being less than in tumor, hemorrhage, or any other focal disease.

It should not be forgotten, however, that brain abscess occurs occasionally without any apparent focal symptoms at all, and sometimes, indeed, with very few general symptoms, the diagnosis being a post-mortem revelation. Brain abscess, unsuspected, is occasionally the explanation of "sudden death."

Abscess of the brain in children under 5 years is rare. The principal causes are otitis and traumatism. It rarely follows acute otitis, most often neglected cases, and is surely secondary to disease of the petrous bone. In the case occurring in infancy without evident cause, the source of infection is probably the ear, even though there be no discharge. The development of abscess after injury to the head without fracture of the skull is extremely rare. In nearly all the trauma cases definite cerebral symptoms show themselves within the first two weeks after the injury. In case of falls, as remote as several months, there is probably some other causes, as a latent otitis. L. Emmett Holt (*Arch. of Ped.*, March, 1908).

**DIAGNOSIS.**—Ordinarily it is quite apparent in patients suffering from cerebral abscess that some affection of the brain exists.

It is by no means so easy always to decide that the symptoms of a given case are due to abscess. The diseases which most often confuse the diagnosis are meningitis, tumor, and sinus phlebitis. The difficulty encountered in differentiating brain abscess from sinus phlebitis and meningitis is increased by the fact that the same causes may operate to produce either of them. This is especially true of trauma and the various infectious diseases, and also of disease of the internal ear, though the latter points to abscess rather than meningitis or phlebitis. In all three the temperature is affected,

but it is usually above normal and sometimes quite high in meningitis and phlebitis, while it is either below normal or quite irregular in abscess.

MacEwen attaches great importance to a persistent low temperature in cerebral abscess in contrast with continued high temperature in sinus phlebitis. This observation has been found only relatively true by others, Okada reporting a decided rise and persistent febrile course in more than one-half of a series of 88 cases of cerebral abscess.

In meningitis the onset is usually more acute, the symptoms more diffused, the delirium is more conspicuous, the tendency to rigidity and generalized spasm is more marked; there is photophobia and a state of widespread cutaneous hyperesthesia with accelerated respirations and irregular, high pulse. Focal symptoms are less common in meningitis except in cases affecting the base, when the number and degree of involvement of cranial nerves is more marked than in cerebral abscess. If the meningitis is localized and circumscribed, I do not believe it is possible to make the differentiation positively. Tenderness of the skull over the site of the disease points to abscess rather than meningitis in such cases. A higher pitch and greater resonance on percussion over the tender side of the skull are considered by MacEwen as indicating abscess, and as of value in excluding meningitis.

In sinus phlebitis the swelling back of the ear with tenderness on pressure and a cord-like hardness of the jugular at times will determine the nature of the condition with little difficulty. Within the past few years lumbar puncture has found some favor as a means of differentiating abscess from meningitis and sinus thrombosis. The

presence of micro-organisms—any one of many varieties may be found—indicates meningitis or sinus phlebitis rather than abscess. The diagnostic value of lumbar puncture is, however, exceedingly negative as yet, and promises to remain so, in the opinion of the writer, so far as brain abscess is concerned, for a very indefinite future. On the other hand, McKernan and other otologists of large experience attach decided and important significance to a marked leucocytosis in suspected cerebral abscess.

Finally, it should not be forgotten that the three conditions of cerebral abscess, sinus phlebitis, and meningitis may coexist, occasionally developing almost simultaneously; under such circumstances attempts to differentiate are obviously academic.

**ETIOLOGY.**—Abscess of the brain is always a secondary condition dependent upon the intracranial invasion of micro-organisms from adjacent or remote sources of infection. Any one of the pus-producing micro-organisms may act as an exciting cause. The affection may occur at any age, but is most frequently observed in adolescence and middle adult life. It is rare in very young children (Holt) and in old age. Males are more often affected than females in proportions varying from 3 to 1 to 5 to 1, according to the observer. By far the most frequent source of infection is purulent disease of the middle or internal ear. More than a third of all cases originate from this source (Pitt). Cerebral abscess is far more common from chronic than from acute suppurative disease of the ear. This fact has been established beyond question by an analytical study of several thousand cases (Jansen).

Next most common cause of brain

abscess is trauma of the face or skull. Practically all cases occurring in very young children are due to one of these two causes: ear disease or trauma.

Among adults surgical diseases of the ethmoid bone, the orbit, the antrum, necrosis of the maxillary bones and sometimes caries of the teeth, disease of the frontal sinus, and pyogenic affections of the nose and throat are occasional sources of intracranial pus infection. Several cases have occurred as complications in erysipelas of the face or scalp. Suppurative adenitis of the cervical glands is another well-known source of infection. Pus accumulations anywhere in the system—even in remote localities, as the liver, the lungs, the Fallopian tubes, etc.—may, by circulatory metastasis, be attended with a complicating cerebral abscess.

The tegmen tympani and the tegmen antri are the two most vulnerable points in the development of brain abscess from acute middle-ear infections. There is an important relationship between the lymphatic ring of Waldeyer and the cavum tympanum. Erosions and depiscences were important in the consideration of this subject. Infection can take place among the emissary veins, or it may travel along the sheath of the facial nerve to the labyrinth and thus to the brain. There is great possibility of development of brain abscess in acute and chronic middle-ear infections. Max Goldstein (N. Y. Med. Jour., June 8, 1912).

The general or local disease on which the cerebral abscess depends is, on the whole, the most important etiological factor, for brain abscess is never a primary disease. The statistics of Pitt, though now twenty-two years old, are still valuable, as they show the proportion of brain abscess to all other diseases. In 9000 autopsies abscess of the brain was found in 56 cases, and the cause of the abscess was: in 18 cases

diseases of the ear and temporal bone; in 8 cases disease of other cranial bones; in 9 cases injury; in 9 cases pyemia; in 8 cases lung disease; in 4 cases the cause was undetermined.

According to Ernst, brain abscess is in 70 per cent. of the cases due to some definite local disease, which in 42 per cent. of cases is in the ear.

The four chief causes of abscess of the brain are: (1) injury to the head; (2) certain general infections; (3) certain local diseases other than those of the head; (4) local cranial suppurations. C. A. Ballance (*Clinical Journal*, Aug. 7, 1912).

Case of cerebral abscess due in all probability to suppurative tonsillitis. The portal of entry for the organism causing the temporal abscess may have been through that portion of the skull anterior to and above the right temporomandibular joint, a spot made vulnerable by the loss of the pericranial membrane. At autopsy the dura and surrounding tissues at a point corresponding to the denuded portion of the bone showed marked inflammatory changes. T. B. Throckmorton (*Chicago Med. Rec.*, xxxviii, 128, 1916).

The brain may be, and often is, attacked in general pyemia and septicemia, and tuberculosis and syphilis affecting the encephalon may present the local conditions of abscess. Various constitutional diseases of infectious origin, among which may be mentioned small-pox, typhus and typhoid fevers, grippe, and cerebrospinal meningitis, are occasionally complicated with brain abscess.

The writers have operated upon 62 cases of gunshot injury of the brain during the past year, with 23 deaths. Among these 62 cases abscess was found at operation in 42. But there were a number of patients who apparently recovered perfectly from the operation, and yet who later developed abscesses and died. Six such cases are described. The abscesses

generally developed 4 or 5 months after the operation; in 1 case the interval was 8 months.

The symptomatology of late abscess is quite characteristic. The patient shows a rise of temperature for awhile, and then suddenly general symptoms develop, such as headache, vomiting, and signs of beginning meningitis. There is apt to be an increase in already existing local symptoms, such as hemiplegia or aphasia. These phenomena are explained by the fact that the abscess has been strictly encapsulated for some time, but finally there has been propagation of the pus to the meninges through a small opening into one of the ventricles. Often when the abscess becomes manifest it is too late to save the patient by operation, but cases can often be saved by early operation.

From the foregoing it is evident that all cases of brain or skull wounds should be kept under careful observation for several months, and if there is a rise of temperature or the slightest sign of cerebral irritation the wound should be opened up. If there is pus, free incision and drainage are indicated. Marburg and Ranzi (*Surg., Gynec. and Obstet.*, from *Neurol. Zentralbl.*, xxxiv, 546, 1915).

**PATHOLOGY AND MORBID ANATOMY.**—Brain abscess is always secondary to the intracranial invasion of pyogenic micro-organisms. The growth of such abscess is steadily progressive except when, as occurs occasionally, a membranous wall of tissue develops, inclosing the pus and preventing its encroachments upon surrounding structures; when so surrounded, the abscess is said to be of the encapsulated variety. When incapsulation occurs the further progress of the disease is temporarily and sometimes for long periods of time arrested. The danger of rupture is always present, however, such rupture resulting in

sudden apoplectiform symptoms with death, the picture simulating a sudden vascular lesion. In its incipency brain abscess presents the local appearance of what has been termed "acute, red softening." Later the pus changes from a reddish-yellow to a greenish or greenish-yellow color, and is at times quite offensive in odor when exposed. The complications usually found are sinus phlebitis and thrombosis (lateral and superior petrosal), leptomeningitis, extensive meningoencephalitis, and purulent pachymeningitis. Leptomeningitis and sinus thrombosis are especially common in cases due to aural disease.

**PROGNOSIS.**—Brain abscess is almost always, if not always, inevitably fatal if treated otherwise than surgically. The duration is variable. The acute cases generally terminate within a week or ten days in death. The slow incapsulated variety may extend over months and even years, the patient dying finally from exhaustion or perhaps suddenly from rupture of the abscess sac. In the slow chronic cases the symptom picture may be that of an insanity, usually of the confusional or demented type.

Case reported a year previously in a boy aged 10 years whose frontal sinus had been exposed through a Killian incision. The frontal sinus had been relieved of considerable pus and thoroughly curetted, together with some anterior ethmoidal cells, and the frontal nasal duct had been enlarged. Some weeks later it became necessary to expose a large epidural abscess leading down to and connecting with the frontal sinus, requiring the removal of considerable necrotic bone. After various tribulations, the patient succumbed a year after the operative procedure. McCoy (*Laryngoscope*, Nov., 1911).

The writer has collected 106 cases, 82 of which were secondary to fron-

tal sinusitis, 11 to ethmoidal disease, 4 to antrum suppuration, and 1 was secondary to sphenoidal disease. Twenty-five cases of cured extradural abscess following frontal-sinus suppuration were on record, and among these there was 1 case in which exploratory puncture of the brain had been performed, with a negative result. In 7 of these cases the posterior wall of the frontal sinus had been perforated, and in 11 cases it was found to be diseased. In 20 of the cases of brain abscess the posterior sinus wall had been perforated, and in 57 of the cases it was diseased. In the majority of the cases the brain abscess was situated in the frontal lobe; three times it was found in the temporal lobe, once in the pedunculus cerebri, and once in the cerebellum. Of these 106 cases of brain abscess, 12 recovered as a result of operation and 29 died in spite of operation. Exposure of the cranial cavity through the ethmoidal cells in life had not yet been carried out. Onodi (*Jour. of Laryn., Rhinol., and Otol., Aug., 1911*).

**TREATMENT.**—Every case of brain abscess should be operated upon and the pus evacuated just as soon as the diagnosis can be made. In no department of brain surgery have results been so brilliantly successful. In a great majority of cases the abscess is easily accessible and can be readily reached. The surgeon should not wait for coma or grave symptoms of irritation or pressure, but should enter the cranial cavity, at least in an exploratory way, as soon as it seems probable that cerebral symptoms in a given case point to abscess formation. In Starr's collection of 419 cases (*New York Medical Record*, March, 1906) there were 197 recoveries, or nearly 50 per cent. In the same paper 79 cases of sinus phlebitis are reported, in very few of which was it possible to differentiate



abscess, of which number 41, or more than half, were cured by operation.

Two cases of obstinate suppuration above the tympanum in which a cure was finally obtained by blowing **boric acid** into the ear, the patient meanwhile reclining with his head hanging over the edge of a sofa, with the affected side down, the mastoid antrum therefore being at the lowest point. This brought the powder exactly where needed. The patient lay in this position for ten minutes, and the procedure was repeated every day, the result being that the suppuration gradually dried up. Mekler (Wiener klin. Woch., July 23, 1908).

The results of operation in 100 cases showed 52 cases resulting in cure, and 48 in death. In 41 cases the abscesses were opened through the tegmen, and, of these, 27 resulted in cure and 14 in death; 37 cases were opened through the squama, and, of these, 18 resulted in cure and 19 in death. In 22 cases the method of operation is not mentioned, and, of these, 7 resulted in cure and 15 in death.

It seems that the best results were obtained when the abscess can be drained through the tegmen. This is due to the fact that the operator by taking this route has been able to open the abscess along its avenue of infection, thus avoiding the danger of secondary meningitis and of hernia cerebri, since as the result of the infectious process the meninges have been soldered together and the subdural space has been obliterated over a given area.

In the case of brain abscess the operator should first search carefully through the tegmen tympani and tegmen antri, and if such a path is found the diseased bone should be removed. If more space is needed the opening should be enlarged upward and outward through the squamous plate of the temporal bone. In incising the dura this incision should be made through the diseased dura, if possible, as here the membranes

will have become adherent. Dench (Amer. Jour. Med. Sci., Nov., 1907).

Brain abscess due to war injuries may in great part be prevented by careful treatment of all head wounds. They should be opened up thoroughly and examined and any foreign bodies removed. The wound should then be filled with loose gauze and left open. Skull wounds should never be sutured, as there are almost certain to be late complications if they are. Subdural hematomata should be treated conservatively; an intact dura should not be opened unless there are urgent symptoms. If a brain abscess forms in spite of these precautions it should be **opened up freely** and the **pus drained out**, care being taken to reach all pockets and recesses. Drainage should be provided with loose gauze; never with rubber or glass tubes. The first dressing should be left 2 or 3 days and after that the wound dressed daily. P. Manasse (Münch. med. Woch., lxii, 1475, 1915).

The writer invariably failed with suppuration following wounds in the brain until he found that a single narrow straight strip of **rubber tissue** drained better and gave better chances for healing when the head was kept up. The dressing should be applied with the patient seated, the pressure in the brain being then much lower unless the brain is actually swollen, which the change of position reveals if present. Barany (Münch. med. Woch., Jan. 26, 1915).

In **trephining** in traumatic brain affections, it is advisable to distinguish late and early cerebral abscess. The late abscess apparently does not arise in the contused part itself, but in a healthy one, just like non-traumatic abscesses after traumatic suppuration in the bones and soft parts. These late abscesses generally lie deep, and are covered by normal cerebral cortex. The early abscesses usually arise in the injured area, into which infective

material penetrates from without. Fatal meningitis is often associated with immediate suppuration. If the suppurative process is slower, however, and the wound in the brain small, adhesions of the cerebral membranes take place in the region of the injury, and abscesses may result. These abscesses are, to a certain extent, the result of retention of pus in the nests and sacs of a deep wound, and are generally superficial and cortical. They do not develop before two weeks. Very early onset of paralysis or symptoms of cerebral irritation, following skull trauma especially, are indicative of meningitis, while the late appearance of symptoms points rather to abscess (Nasse). These apparently refined details are at times of extreme importance in view of the fact that surgical intervention is the sole resource, and of the further fact that localization of the abscess, often a matter of great uncertainty, is essential to success. While mathematically exact localization is desirable, approximate localization is often sufficient, since it is the accepted procedure by all surgeons of experience to expose as large an area of brain surface as possible. The contributions to the literature of this subject which will be found of especial value are those of MacEwen, Jansen, Korner, Bacon, and McKernan.

The writer lays stress on early detection of the abscess and its correct localization as the chief factors conducive to success in the treatment of these cases. Very often a case of otitis media, especially if it has been treated by the mastoid operation, is regarded as being well when it is not really well; chronic otitic cases should be watched both from the bacteriological point of view (blood-counts and opsonic tests) and the

neurological standpoint. In most instances the reflexes on the opposite side of the body will be found altered in chronic otitis. The more frequent performance of a bone operation is advised, because all records of abscess in the adult go to show that it is due to prolonged infection of the bone. As to the early detection of cerebral disease, excluding sinus thrombosis, the chief difficulty is the distinction between abscess and meningitis. The following differential points are mentioned: 1. Regular and full pulse in abscess, in contradistinction to an irregular and relatively small pulse in meningitis. 2. Depression of temperature,—a sign the value of which has not been properly appreciated. As a means of localization of the abscess, and to decide whether it is single or multiple, temperature observations are also valuable; if a lesion is situated in the coronal plane through the Rolandic area, the temperature, owing to the proximity of the abscess to the heat centers, rises on the opposite side of the body, whereas if the abscess is either anterior or posterior to this level no such change takes place. 3. A graded hemiplegia, the face being most involved, then the arm, trunk, and leg in order, points to abscess rather than meningitis. If pressure is being exerted on the Rolandic area posterior to the coronal plane through the Rolandic fissure, then, although the motor paresis may be almost unnoticeable, there will be detectable a delicate loss of the sense of localization of position (*i.e.*, of the point touched), which is a valuable early sign in otogenic abscess in the temporal lobe. 4. In meningitis the superficial reflexes soon disappear and are bilaterally affected, whereas in abscess they are unilaterally affected, and disappear late. Changes in the abdominal reflexes precede and continue for longer than the changes in the knee jerk. 5. As regards optic neuritis, examination of a large number of cases showed that

the meningitic patients present a highly edematous, swollen disk in contrast to a very moderately swollen disk in the case of abscess. A perfectly bilateral neuritic change is a typical accompaniment of meningitis; on the other hand, in abscess there is an overfilling of the retinal veins, limited to one side. Treatment is adequate drainage and vaccination. For the drainage always employ concentric tubes; as far as possible, no tube is removed from the wound until the final granulation occurs. Horsley (Proceed. Royal Soc. of Med., Feb., 1912).

One of the difficult things in the treatment of a brain abscess, is to find a drain that does not soon clog and cease to be of use. It is hard to keep an ordinary brain drain in place. A wire drain tends to catch in the granulations at the edge of the skin wound and holds in place almost too well, but the **copper gauze** allows the operator to bend the drain as he pleases. For insertion it is closed by a plunger. The natural shape of the drain is a cone. If the drain is kept clean it serves in a measure the purpose of an encephaloscope, as the brain substance or the wall of the abscess can be seen to a certain extent through the meshes of the wire gauze. H. P. Mosher (Trans. Amer. Otol. Soc., vol. xiv, part 1, 1916).

Case of extradural abscess complicating an acute left frontal sinusitis, which early drainage of the frontal sinus through the nose would possibly have averted. The infection advanced by way of the blood stream or lymphatics. The rapid and alarming symptoms which appeared were those of a circumscribed purulent leptomeningitis, doubtless brought about by the dura mater becoming perforated in one or more places, thus allowing the pus to empty through. W. W. Perdue (Med. Rec., Jan. 15, 1921).

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## CEREBRAL HEMORRHAGE.

**—DEFINITION.**—Under this head are classed all cases in which there is an effusion of blood due to the rupture of some vessel within the substance of the brain proper or in the pia. This hemorrhage usually starts in the brain, but may force its way out and become subarachnoidal or ventricular. Except in case of accidents, it rarely makes its way into the subdural space.

The dural system of arteries is quite distinct, and bleeding from this source should be considered separately.

Simple tingeing of fluids about the brain, not coming from any blood-focus, does not constitute a cerebral hemorrhage in the strict sense.

**Varieties.**—It is customary to classify these cases according to the part of the brain that is the seat of the hemorrhage, as cortical, subcortical, or of the central ganglia; frontal, or of either lobe, pontile, cerebellar, etc. Besides the above, however, there are several subforms, as:—

**Ingravescent.**—This is a term applied to large effusions developing slowly, *i.e.*, for a period of several hours or for a day or two. This form is largely observed in hemorrhage at the external capsule; the peculiarity is due, first, to rupture of a large perforating artery that passes up at this point, and, second, to the parallel course of the nerve-fibers in this tract whereby they continue to separate as the pressure increases.

**Symmetrical.**—Here there is a double hemorrhage, starting from corresponding points of the two hemispheres.

**Meningeal and Ventricular.**—These forms may either start as such—though rarely—or they may start from vessels in the brain-substance and then rupture

through into one or the other of these spaces.

**Traumatic.**—Due to violence or injury, in contradistinction to the general run of spontaneous cases.

**Punctate and Capillary.**—These are sufficiently explained by the terms. Of themselves they are rarely of sufficient moment to be of other than pathological interest.

**SYMPTOMS.—Prodromata.**—The so-called premonitory symptoms include headache, dizziness, pallor or flushing of the face, fullness in the head, flickering before the eyes, visual obscuration, disturbed sleep, tinnitus aurium, thickness of the tongue, numbness or peculiar tinglings of one side of the body, heaviness of extremities, slight mental changes,—as lapses of memory, drowsiness, and irritability,—changed, slowed, or intermittent pulse, nose-bleed, etc.

Clinical histories of 5 cases showing: an extreme degree of vertigo at the onset, which gradually subsided to some extent, but which recurred on any attempt to walk, and which also remained as a permanent symptom; an uncertainty in gait, which was due not to paralysis, but to a lack of balancing power, which resulted in staggering and uneven steps. There was also an unnatural posture of the head when at rest, and nystagmus. When these occur together these symptoms are characteristic of cerebellar disease. Starr (Med. Record, May 12, 1906).

In a study of the serodiagnosis of cerebral hemorrhage, the writers found that certain serums were greenish and more or less fluorescent and that the serum always came from a patient with cerebral or meningeal hemorrhage. In 3 other patients with symptoms suggesting cerebral hemorrhage, but which proved to be softening of brain and no hemorrhage, there was no green-

ish tint to the serum. Marie and Leri (Bull. de l'Acad. de Méd., lxxviii, Nos. 21-22, 1914).

These symptoms, when occurring in an elderly person, are thought by many physicians to forebode an impending hemorrhage. There is no doubt that such symptoms frequently precede thrombosis. This fact, together with the lack of adequate pathological proof and inability to account for premonitions in hemorrhage, has caused a disinclination among conservative observers to recognize any connection of the kind. In some cases, however, there may be a preliminary oozing sufficient to produce slight symptoms. Further, the evidence of a vasomotor influence suggests that a local paralysis of vessels with sufficient dilatation to irritate the adjacent tracts may precede the actual rupture. This, however, in a few days ends in a frank attack of apoplexy. In the aged most of these symptoms point rather to thrombosis; but in earlier years they may, possibly, in rare cases, give warning of incipient hemorrhage.

Series of 5 consecutive cases of apoplexy which showed a marked periodicity in their recurrence. The danger periods appeared not to exceed five days and recurred at approximately 30-day intervals. The writer suggests that the phenomenon may be due to: 1, influences originating in the nervous system; 2, the products of germ or parasitic activity; 3, mechanical compensatory changes of blood-pressure; 4, disturbance of metabolism, assimilative or eliminative, or, 5, to the function, or disturbance of the function, of a gland or chain of glands possessing an internal secretion. Hurst (Jour. Amer. Med. Assoc., Feb. 3, 1912).

Constipation is common in the prodromal stage, but is too usual a matter to have any diagnostic significance.

Turgidity of the vessels of the head, severe pain in the head, convulsive twitchings of an extremity (Jacksonian), unilateral chorea, etc., are rare, and belong to the initial stage of apoplexy—or, of course, more often its later stages.

*Onset.*—The symptoms that may mark the onset of the attack include the various prodromata just mentioned; also faintness or general prostration, convulsive movements, aphasia, paralysis, stupor and even unconsciousness, free perspiration; slow, tense pulse, etc.

The regularity and the sequence with which these appear are very variable. In fulminant attacks the severest symptoms may promptly develop, and even death itself be not long delayed. Sudden death is very unusual, but may occur if the trouble is in the pons. Oftener there is a gradual increase, both in the number and the severity of the manifestations, for some little time: one, two, three, or more hours.

*Headache.*—Very often there is no special complaint of pain in the head, and, again, headache has been such an habitual thing with the patient that little importance can be attached to it. Nephritic complications, when present, tend also to rob this symptom of value.

In many cases, however, there is headache, severe, deep, and general in character, less often localized. It becomes more pronounced as the effusion increases in volume, and, even when the consciousness has become more or less obscured, the sufferer may persist in putting a hand to the head, evidently because some degree of pain or distress is still perceived.

When, therefore, we meet a headache which is unusual to the patient, excruciating in character, not otherwise

explicable, and associated with suggestive phenomena, it acquires some value as a symptom.

A low, occipital pain is common in cases of cerebellar apoplexy; but as it is far oftener due to other causes its only significance comes from association.

*Vomiting.*—This is a common symptom and one of much clinical importance, its value, however, depending much on the certainty with which uremia can be excluded. Nausea may, of course, attend dizziness, faintness, or thrombosis; but actual vomiting, aside from uremia (especially if the person is reclining), argues, in a suspicious case, for hemorrhage. This applies to the increasing period of the effusion.

It has been claimed to be especially frequent in cerebellar hemorrhage, but, as stated, it is common in all forms.

Where the latter is at all voluminous, in almost any part of the brain we see vomiting, often severe and even somewhat prolonged. Its occurrence depends upon the volume of the effusion, the speed with which it is poured out, and to some extent upon its location; also, like the motation, on the wider circulatory effect. In the slower, or ingravescient, forms, even though they finally reach a large size, there is less tendency to emesis. It is where we find other evidence of an apoplectic seizure that this symptom acquires value; then it also assists materially in differentiating the nature of the brain-process.

Nearly always some other plausible explanation is proffered: the person has just eaten overheartily, been lying in a cramped position, had an hypodermic, taken medicine that upset the stomach, or been suffering from gastric catarrh. The diagnostician must, of

course, be able to discount such suggestions.

*Yawning and Sighing.*—These are very frequent and striking symptoms in hemorrhage, and are often more marked if the patient is in a sitting position. There is a slight parallelism between them and the vomiting. But as they are also common in cases of thrombosis and may occur in embolism while there is a badly damaged heart, they have only a limited diagnostic value. In cases of hemorrhage these manifestations suggest that the focus has already reached a sufficient size to produce some degree of brain anemia.

*Coma and Other Disturbances of Consciousness.*—These are of great importance for both the positive and the differential diagnosis. But at the same time they are matters most difficult to describe or define with exactness and in accordance with the facts.

Coma is a state of profound unconsciousness not due to sleep, syncope, hypnosis, or drugs. But in practice we meet all kinds and degrees of disturbance of consciousness. The eyes may be open and staring, yet the person fail to make any responses to our interrogations and evidently fail to have any understanding of language or surroundings. More often there is a condition of stupor that admits of but partial and temporary recognition. We can then conveniently distinguish coma, stupor (a partial coma: "semicomatose"), and dazed conditions.

The duration of these states is next in importance. They may be of such transitory nature as to pass unnoticed, or they may last several hours or days, the lighter degrees being, of course, as a rule, of shorter duration. The time in the attack when coma supervenes is also to be noted; if at the start it may

be partly a direct shock-effect; if later and more gradual it indicates that the effusion has reached a large volume.

The size of the output requisite to produce this symptom varies much with its location. A small clot in the pons, for instance, will produce a much deeper impression on consciousness than one of far greater size in the pallium. Wernicke and others have sought to explain this by the smaller size of the vessels, their indirect course, and hence slower leakage in the hemispheres. But this view is negated by several facts, however well it may explain the favorite sites of hemorrhage.

The comparison of a large number of these cases shows that involvement of the sensory tracts has little or no influence on consciousness, while other cases with equal-sized foci involving certain parts of the motor path show, as a rule, very marked impairment of consciousness. From a psychological standpoint this seemingly anomalous fact agrees with conclusions based on other evidence. But it is cited here to prove that much depends on the part involved as to the effect on consciousness. The question of waking and sleeping centers has recently been reviewed.

A close analogy can also be drawn with cases of embolism. The writer has shown that embolism involving only parts above the central ganglia does not cause coma. Inasmuch as in many of these cases a large patch of brain-tissue is involved, and as, further, the suddenness of the attack must be equal, whatever the part involved, it follows that here again much must depend on the particular structures included, for smaller infarctions, if only they involve the ganglia, often do bring on coma.

It can consequently be stated that,

whatever accessory influences there may be, there are but two important governing factors in the development of coma: the size of the hemorrhage and the particular part of the brain implicated. These deserve a little further consideration.

As to the amount of hemorrhage that will of itself cause coma, experiments on animals by Pagenstecher, von Schulten, and others have led to the conclusion that in the human being one and a half to two ounces are about the extent of limitation of the brain-space that can be borne without interruption of psychical functions. (More can be tolerated in a diffuse effusion like a meningeal hemorrhage than in a confined focus.) The exact amount thrown out in a case of apoplexy is rarely, if ever, known, since some of the fluid is promptly absorbed or scattered, and, independent of that, it is impossible to more than estimate the volume of these irregular foci. So far as such rough estimation goes, it corresponds fairly with the experimental results. This applies to cases in the hemispheres (pallium). When the size of an effusion is stated to be that of a hen's egg, it may be considered to equal two ounces of fluid. Hence, hemorrhage of that bulk should be, and in practice is found to be, on the border line. It may be expected to at least produce stupor and frequently some coma. When of greater volume, coma very generally results. In the basal ganglia, however, a much smaller amount may suffice.

The principle here is that the effusion, by its volume, exerts such a general pressure on the whole cortex as to obtund consciousness. Of the sufficiency of this factor there is no question. It may act by producing an an-

mia or by more direct mechanical effect.

As to the susceptibility of different parts, injury below the oblongata (*i.e.*, in the cord) does not cause coma. The syncope of shock or even sudden death may result, but not real coma. And it is uncertain whether hemorrhage of the oblongata has much tendency to produce coma; most such cases are small, and any stupor is masked by respiratory and other phenomena. In the old case of Fabre (quoted by Gintrac and others) some loss of consciousness attended a small hemorrhage of the left pyramidal body. But in several other cases of small effusion in other parts of the oblongata no distinctly comatose condition has developed.

At the other brain-pole—*i.e.*, cortical of the central ganglia—we have already seen that coma is essentially a consequence of general brain compression. In this major portion of the encephalon there is little difference between the various parts. Apparently the occipital lobe tolerates infringement better than the frontal and parietal lobes; but there is no decisive difference.

Regarding the cerebellum, the general opinion agrees with the evidence that uncomplicated hemorrhage when moderate in amount does not invoke coma. But in these rather rare cases either rupture occurs or, if much size is attained, there is so much pressure on subjacent structures as to obscure the bearing of the case.

There still remains the region of the central ganglia, the cerebral crura, and the pons. Hemorrhage of the caudate nucleus is prone to bring on coma. That in the lenticular nuclei and in the thalami is somewhat less apt to do so. When in a cerebral crus, there is commonly some coma or, at least, stupor,

though these hemorrhages are rarely voluminous. Those of the pons are most inclined to cause coma, though usually small unless they have already ruptured. A comparison of this last group of cases (involving the brain-stem) brings out forcibly one fact already referred to, viz.: that hemorrhages in the sensory path show but little tendency to cause coma, while those in the motor path have a marked tendency in that direction. This fact stands out quite as clearly when they are compared by volume. So far as this coma zone has been noticed in the past, it has been thought to depend upon the fact that here were grouped fibers passing to, and thus influencing, all parts of the brain.

*Secondary Factors in the Causation of Coma.*—There are, of course, various other influences that affect this result. The person's susceptibility is one; carbonic acid poisoning due to superficial respiration is another. But most important of these is the rapidity with which the effusion occurs. On the experimental side it is well known that the effect on consciousness depends somewhat on the rapidity with which the compression is produced. But it is rare in clinical work to meet cases where a hemorrhage has taken place with any such rapidity as in the average experiment. As Liddel long ago pointed out, considerable time is taken up before the bleeding stops. We also know that in the slow, ingravescent form, though a day or two elapse in the process, coma just as certainly supervenes when the volume of the focus becomes adequate.

The disappearance of coma is attributed to a re-establishment of the circulatory balance, to reduction of pressure from lessened cerebrospinal fluid,

and perhaps a gradual tolerance to the focus. The shock-effect passes off, and some of the fluid of the focus is absorbed.

Complete and persistent coma in cerebral hemorrhage is not due to entrance of blood into the brain ventricles. From pathological studies they are convinced that in coma there must be a suspension of the functions of both cerebral hemispheres through compression by the blood, i.e., the uninvolved, non-hemorrhagic hemisphere must be compressed against the unyielding cranium by the increased volume of the hemisphere in which hemorrhage has taken place. Pierre Marie and Léon-Kindberg (*l'Presse méd.*, June 6, 1914).

*Aphasia.*—This symptom, of itself and without corroborative manifestation, is rarely indicative of cerebral hemorrhage. A considerable majority of all cases of aphasia are due to other causes (see article on APHASIA, vol. i). These are mostly transient forms lasting from a few hours to a few days and embracing all degrees of speech impairment up to its complete loss. They are occasioned by gout, uremia, and less frequently other toxic conditions. Possibly the standard writers do not take sufficient notice of these transient forms. Even of the more lasting cases a certain number will be due to thrombosis, embolism, etc.

Only in a part of the cases of cerebral hemorrhage do aphasic symptoms appear. To produce these the speech tracts or centers must either be directly injured by the effusion or indirectly implicated by pressure. This, of course, only occurs when, in right-handed persons, the lesion is on the left hemisphere, and in left-handed in the right hemisphere. Apparent exceptions to this rule occur, as in a recent case (of embolism) where an original left-



handed youth had so trained himself that he passed for a right-handed person.

All degrees and forms of aphasia occur in association with hemorrhagic apoplexy. Where it is due to implication and not to direct involvement of the speech-center or tract, recovery from this symptom may occur, the time required and the extent of recovery being dependent on the circumstances of the case. By speech-center we, of course, mean not only the motor center in Broca's convolution, but also the hearing center and other associated parts. Inasmuch as all forms of aphasia and paraphasia are involved, it is not practicable to enter on a discussion of them here.

*Convulsions, Twitchings, Motation, etc.*—Rarely a few spasmodic twitches occur during the onset period in the territory where paralysis is developing. These may not be noticed unless in the face. It is not certain that they point to a cortical focus.

Quite distinct from these are the unilateral clonic convulsions (Jacksonian type) that occur in the rare cases of effusion about the cortical motor area. Such cases are far oftener of traumatic than of spontaneous origin.

The apoplectic motation described by the writer (1904) is a general and not unilateral restlessness occurring during all the developmental stage. It consists of a continued series of small movements by one and another part of the body. It has a double value, first aiding in differentiation and then telling when the hemorrhage has stopped.

Of course, uremic convulsions may bring on or accompany an apoplectic seizure, though this is unusual. Otherwise general convulsions in this condition point strongly to ventricular hem-

orrhage or to rupture into the lateral ventricles. They also are not rare in thrombosis, and in both meningeal and frontal hemorrhages.

Even in case of such rupture, however, convulsions do not always follow, nor does slight oozing, as in many cases of impending rupture, have this effect. When such convulsions do occur, they may be of the severest character that we ever witness. In any case, such complications give a very bad outlook, for ventricular rupture is only more certainly and rapidly fatal than uremia. Rigidity of the paralyzed or even both sides is also frequent in ventricular rupture.

Report of 10 cases bearing on the question of the correctness of the assertion of Dejerine, Strümpell, Brissaud, and Leube, that convulsions and rigidity in apoplectic hemiplegia point to the rupture of the hemorrhage into the ventricles, and also on the possibility of stimulation of the axons of the upper motor neurons when they are separated from their perikaryons. The writer summarizes his conclusions substantially as follows: 1. Ventricular inundation in cerebral hemorrhage has no etiological bearing on the convulsions or rigidity. 2. Tentatively, and basing his opinion on the 10 cases, he concludes that the convulsions and rigidity in apoplectiform hemiplegia are frequently due to involvement of the optic thalamus or corticothalamic sensory fibers, provided, of course, that enough of the posterior limb of the internal capsule remained intact to convey the motor impulses. 3. Convulsions and rigidity in apoplectiform hemiplegia may be caused by a sudden or rapid increase of intracranial pressure from cerebral hemorrhage, even if the thalamus and corticothalamic sensory fibers are uninvolved. In this case, also, there must be a sufficient portion of the internal capsule left uninjured to convey the motor

impulses to the parts concerned. 4. It is altogether unlikely that pressure or chemical change, acting on the motor axons of the centrum or internal capsule,—these axons having been severed from their perikaryons by the hemorrhage,—could exert a sufficient stimulating action to cause convulsions or rigidity. Allen (Jour. Amer. Med. Assoc., July 18, 1912).

*Paralysis; Respiratory Paresis.*—

This is one of the commonest as well as most striking and characteristic symptoms, although not a necessary accompaniment. It may affect either motion or sensation or both.

The time of the attack at which hemiplegic symptoms develop depends on the location and the rapidity of development of the effusion. Usually it appears with the onset of the seizure, though at first frequently but a mild degree of paresis; in such a case we can conclude that, as yet, the motor path is only suffering from pressure. In occasional cases the paralysis is not manifest until later or becomes pronounced only in the reaction stage; but it is then difficult to distinguish from an increasing effusion.

Series of 14 cases—8 with autopsy—which leads the writer to believe that intermittent paralytic conditions sometimes occur due to an irritable state of the walls of a cerebral vessel, this condition resulting in repeated sudden occlusion of the vessel and suspension of function in the tissues supplied by it. Such attacks of paralysis may or may not be accompanied by transient aphasia. Instead of complete motor hemiparalysis there may be only hemiparesis or a very slight weakness. At times there occur repeated attacks of paresthesia on one side, each attack usually leaving slight feebleness on that side. After a certain number of brief attacks, the subsequent ones show a tendency to greater duration, with the motor phenomena becoming

more conspicuous. Among the causes of these transient contractions of the vessels the most important is the vascular degeneration due to syphilis, alcoholism, and lead intoxication. With years, an actual diseased condition of the vessel walls is established, with thrombosis as final result. The intermittent apoplectiform attacks could thus be considered as premonitory warnings of eventual complete occlusion. Alfred Gordon (Va. Med. Semi-Mthly, Sept. 7, 1917).

Motor involvement constitutes the most marked and important manifestation of average cases, and when present may range all the way from the slightest degree of weakness up to complete flaccidity. While any of the voluntary muscles may suffer, certain prevalent types can be made out. Monoplegias and more limited paralyzes, running as such from the start, occur in some of the rare cases of hemorrhage cortical of the internal capsule. When this is in the occipital, frontal, or temporal lobes, there may be no definite paralysis unless the focus becomes so large that the transmitted pressure affects the motor neurons. But, as the great majority occur in the basal ganglia or pons, the hemiplegic type is by far the most common. Of this there are two distinct forms: the one of simple hemiplegia, where all the affected parts are on one side (arm, leg, and face, all or in part), and the other of crossed hemiplegia, where an arm-and-leg paralysis on one side is associated with some involvement of the cranial motor tracts on the other side. This latter form is typical of localization in the pons, because of the fact that the cranial tracts have already decussated, while the first form is that due to the common site in the basal ganglia. In the very rare cases of bleeding in a cerebral crus, there may be a special form of crossed paral-

ysis: involvement of the arm and leg on the side opposite the lesion and oculomotor paralysis on the same side, due to the intimate relationship of this nerve with the crus.

Study of 5281 cases of cerebral hemorrhage, thrombosis and embolism, and hysterical hemiplegia from the point of view of the side of the lesion or of the hemiplegia showed in 3539 cases of these the nature of the lesion was definitely determined by post-mortem examination. With none of these conditions was any evidence obtained to indicate that either the lesion or the hemiplegia is more apt to affect one side rather than the other. The general teaching to the contrary is therefore not founded on any critical testimony. E. Jones (*Quarterly Jour. of Med.*, April, 1910).

There is some basis for the view that lesions of the thalamus *may* present a special characteristic. This consists of loss of emotional or pantomimic movements, while the volitional motions are still preserved. This applies specially to the cranial distribution. If, on the contrary, the cranial paralysis is due to lesions more anterior at the same level or higher up there may be a preservation of the so-called mimic, with a loss of voluntary movement. In practice, hemorrhages of this region are usually so massive that both grades of motion are equally lost.

It is possible that something of the kind also holds for the extremities, since we sometimes see cases of hemiplegia where, in sleep, the patient is able to lift a hand to the head. Here may also be classed the so-called met-hemiplegic movements; these are such as occur in a paralyzed part in association with voluntary movements in the corresponding well part.

In ordinary hemiplegia we find the arm and leg motionless or nearly so, a

little motion possibly remaining in the fingers or toes. The arm lies helpless by the side or across the chest. The patient, if requested to move it, reaches over with the other hand. The leg stays in almost any position in which it is placed. In the complete form it is impossible for the patient to turn in bed or to rise at all from the recumbent position. In coma the paralysis may be presumed from the drawn face, expiratory puffing of one cheek, and the heavier, passive drop of the affected arm when lifted and let go.

As a rule, the leg improves faster than the arm, perhaps, as claimed, because the arm tract is apt to be more involved than the leg, or, perhaps, because the leg movements (as in walking) are more automatic in character. It is considered an unfavorable omen when, on the contrary, the arm improves faster than the leg. The hypoglossal and facial tracts are more apt to escape direct implication, and the upper facial quite regularly escapes (a point of distinction from like hysterical paralysis).

Sensory loss is also a common, though less frequent and lasting accompaniment than motor. In many cases it is so transient that in a few days little trace of it remains. Its occurrence depends on interference with the sensory neurons. Their most exposed point is at the *carrefour sensitif* (posterior border of the internal capsule), where the sensory tracts are more closely grouped than elsewhere in their course. This point is also about opposite the commoner sites of hemorrhage, though a little to one side, which harmonizes with the fact that permanent loss of sensation is the exception. The most marked features of this type are loss of common sensation in the opposite

half of the body and homonymous hemianopsia (blindness of opposite half of visual field of each eye). Hearing may also be interfered with and sometimes taste and smell, the latter two only on the opposite side. In hemorrhages involving either the hearing center in the first temporal gyre, the visual center in the cuneus, the other sensory center, or the paths connecting these with parts below, there will be a corresponding limited loss of sensation. In pons lesions the special senses escape, unless occasionally those of hearing or equilibrium. At the same time the tracts for general sensation to the other side of the body may suffer. In cases where there is more lasting anesthesia it involves deep parts and mucous membranes as well as the surface.

*Eye Symptoms.*—Pupillary changes have but little value here for purposes of localization. They do, however, serve one important and usually overlooked purpose: the presence of anisocoria (inequality of the pupils) is valuable objective evidence of the existence of some real lesion, and has a bearing on differential diagnosis. Of course, this presupposes the existence of corroborative symptoms and the recent acquisition of the inequality. The possibility of latent anisocoria should be excluded by determining whether the condition persists on full illumination of the two eyes; if, on so testing, the pupils become equal, the inequality can be put down as probably an affair of long standing or spinal in origin.

Inequality of the pupils may occur in large effusions that by pressure weaken the oculomotor on that side and thus allow that pupil to dilate. It is consequently not rare in cases involving the frontal lobe or basal portions of the cerebrum. In pons troubles anisocoria

is common, though both pupils may be large or small according to the degree of third-nerve involvement. In meningeal forms the pupils are often affected, though there is no rule here for our guidance.

Conjugate deviation of the eyes very often points to a lesion on the same side, but this is not an invariable rule.

Diplopia or more distinct evidence of paralysis of external ocular muscles is unusual except in comatose conditions. Its interpretation depends on the individual case.

Ophthalmoscopic changes are not sufficiently marked in the early stages to be of any value, nor are they often much more so in the later. After development of the full apoplectic state there may be some choking of the retinal veins, especially on the side of the lesion. Miliary aneurisms have been observed in the retina, but are quite unusual. Hemorrhages of the retina may indicate nephritis; but only to that extent suggest the cause of any cerebral condition.

*Bowels.*—Constipation frequently precedes or accompanies the attack. Or, on the contrary, where there is deep unconsciousness or prolonged stupor, and especially if drastic purgatives are given, involuntary discharges may occur. Their chief importance lies in the necessity, then, of scrupulous care lest eczema and bed-sores develop, and in the commentary they offer on the state of consciousness or the possibility of dementia.

*Urine.*—At the onset the urine is usually acid. Transient glycosuria is a possible accompaniment of hemorrhage in any part of the brain. The sugar usually disappears from the urine in from a few hours to a couple of days. Presumably it originates from shock to

the so-called sugar-center. When this spot in the floor of the fourth ventricle is directly involved, the sugar may persist longer, though it usually subsides, even then, in a week or two.

As a part of the same manifestation there may be a polyuria simply, that is then even more fleeting in character.

Albuminuria is a frequent and more serious accompaniment. Like the preceding symptoms, it may be but transient in character; but its presence is always a cause for anxiety. Many cases of apoplexy are due to Bright's disease, and an examination of the urine, therefore, should be a routine procedure in all cases.

Case in which albuminuria occurred as a symptom of meningeal hemorrhage. The case was that of a woman of 54 who complained of sudden malaise with general chilliness and severe headache, but no loss of consciousness, merely some torpor. In the liter and a half of urine voided during the twenty-four hours, 20 Gm. (5 drams) of albumin per liter (quart) were found, but there was no tendency to edema or *bruit de galop*, although there was slight fever. Lumbar puncture revealed a typical and abundant meningeal hemorrhage; all the symptoms gradually subsided and by the ninth day there was no trace of albuminuria. In none of the similar cases on record was the amount of albumin over half this proportion. The discovery of large amounts of albumin in the urine without other signs of nephritis may aid in the differentiation of meningeal hemorrhage. In a second case the writers based the diagnosis on this sign alone. This was confirmed by the autopsy. G. Guillain and C. Vincent (*Semaine méd.*, Oct. 27, 1909).

*Hemichorea*.—This is of rare occurrence. It may either precede the attack (prehemiplegic chorea), though this is unusual where hemorrhage is the cause,

or it may develop during the recovery stage (posthemiplegic). It is thought to be due to irritation either of the motor tracts or else of some band of fibers closely associated with these. It is a symptom of irritation rather than of destruction, and, hence, is never present where the paralysis is complete. If an inaugural symptom, it disappears as the paralysis deepens; otherwise it comes on as the paralysis begins to mend, and in turn also disappears as the paralysis wears away. Hence its appearance in convalescence is a good omen, however annoying to the patient. It is not a symptom of the attack itself.

This affection involves strictly one side of the body only. It may take in principally an arm or the lower extremity, but usually involves both more or less. In degree it varies much according to the stage; but is often severe and continuous in character. The type of movements is hardly different from that of ordinary chorea of childhood.

*Tendon-reflexes*.—At the onset and during the period of development no great changes in the reflexes can be made out, unless diminution. But so soon as the effusion seriously interferes with the motor path and even more after the subsidence of shock the tendon-reflexes of the paralyzed parts show a decided increase; this may apply both to the force of the reflex and to the extent of area from which it is elicitable. In gross lesions the pathological jerks like ankle-clonus and wrist-clonus may also be demonstrable, either immediately and temporarily or later on after descending degeneration. Hedit claims that the toe-sign appears on the paralyzed side within a few hours. It is necessary to compare the two sides to settle the relevancy of the

symptoms. Even then there are cases in which both knee-jerks are increased from unilateral lesion, in proportion, perhaps, to an incomplete decussation of the pyramidal tracts, as is further shown by the somewhat bilateral paralysis of the lower extremities. As a rule, however, we find a purely unilateral exaggeration of the tendon-reflexes.

**Other Symptoms.**—Those pertaining to the period of the seizure are almost described by their enumeration.

A slightly subnormal temperature (one to two degrees in rectum) may frequently be found for an hour or two after the onset. Later an increase of temperature is not unusual; notably, it is claimed on the paralyzed side. It amounts to but a few degrees at most and is transient in character, lasting only a few hours, as a rule. These variations in temperature are somewhat commensurate with the severity of the seizure. From the experiments of Ott and others it is known that there are so-called heat-centers as far cortical as the caudate nucleus, and it is to disturbance of these that the hyperthermia is doubtless due. It is claimed for pons hemorrhage that the temperature may rise from the start.

Spinal puncture rarely aids in diagnosis, and is liable to increase the focus of hemorrhage.

Lumbar puncture employed in the diagnosis and determination of the prognosis in cerebral hemorrhage. In 7 cases admixture of blood to the cerebrospinal fluid indicated very serious conditions. When the hemorrhage into the brain occurred suddenly, the gravity of the case depended on the amount of blood pouring out into the tissues and into the cerebrospinal fluid. When the cerebral hemorrhage occurred more insidiously, the symptoms were mild

at first, but they increased rapidly in gravity from the reaction on the part of the meninges, etc. The presence of blood in the cerebrospinal fluid in this class of cases warns of impending danger, notwithstanding the mildness of the symptoms at first. The discovery of blood in the spinal fluid further serves to differentiate cerebral hemorrhage from conditions which might otherwise be confounded with it, such as embolism, congestion, epilepsy, encephalitis, and uremic and diabetic coma. Rossi (*Riforma Medica*, April 17, 1911).

Trouble in swallowing (dysphagia) may be simply an expression of the general weakness, though at times it seems to partake of the nature of a central paralysis. It necessitates extra care lest food slip down the trachea.

The respiration is often affected. Stertorous breathing is an attendant on the deeply comatose state. In the subsequent weak condition of the severe cases Cheyne-Stokes respiration may appear at any time and is especially prone to do so in the hours of deep sleep. It may also occur in the primary coma.

Sphygmomanometry proves to be a doubtful aid in diagnosis; there are no safe rules for the interpretation of findings. A low systolic pressure in the onset stage may help to exclude hemorrhage. On the other hand, a high pressure is so common at this period of life, even in developing thrombosis, as to deprive it of much value. As to the late or chronic hemiplegic state, Tilney's work (1907) showed that the pressure "is very often excessively high." It is as an immediate guide in therapy that this method has chief value here.

Sixteen cases of cerebral hemorrhage in which blood-pressure examinations were made showed the

following facts: Patients with high-tension pulse, no kidney lesion, and no previous hemorrhage are least likely to suffer from increased pressure. Patients with kidney lesions which will not respond to treatment or whose blood-pressure will not lessen are liable to fatal uremia. Nephritic patients with increasing blood-pressure are especially liable to cerebral hemorrhage. Increased blood-pressure without a kidney lesion is more liable to terminate in hemiplegia than the one with such lesion. Nearly half of all patients with increased blood-pressure have hemiplegia; 50 per cent. have hemorrhages. A second hemorrhage with hemiplegia due to hemorrhage already existing, but with no kidney lesion, is usually fatal. Patients with nephritis and increased blood-pressure are as liable to succumb to the second hemorrhage as to live. Second hemorrhage occurring when both hemiplegia due to a former hemorrhage and nephritis exist is seldom fatal.

While increased blood-pressure bears a striking relation to cranial hemorrhage, it must not be used as an infallible sign of such an occurrence, but must be weighed in relation to other existing conditions. Sawyer (Ohio State Med. Jour., Nov., 1908).

The subsequent mental condition often shows impairment of intelligence, psychological functions, memory, and mental grasp. The loss inclines to be the greater, the severer the attack. Laughing or crying on inadequate provocation, an anxious haste in carrying out anything planned, and many other aberrations might be cited.

Case in which mania developed as the patient was recovering from the phase of weakness of muscles and mind which follows a cerebral spinal hemorrhage. The patient was a woman of 82 in whom the muscular weakness lasted about two weeks after the apoplexy, which was fol-

lowed by a week of increasing strength and liveliness, the latter gradually amounting to actual mania with insomnia. This phase lasted for twenty to twenty-five days and gradually subsided, normal conditions being then restored except for persisting hemiparesis. The second patient was a man of 42. The asthenia lasted three or four days and the mania ten or twelve, but there is still a little mental impairment. In 3 other cases the asthenia and mania recurred occasionally and the mental condition compelled institutional care in some. These patients were 42 and 43 years old and their affection merges into periodical depressive mania. Another patient had an attack of melancholia at 27 and a cerebral hemorrhage at 32, followed by recurring attacks of asthenia and suicidal depression, but no actual mental impairment. The literature on the subject of apoplexy in the history of the insane tends to show and the writer concludes that institutional care is seldom necessary for persons developing this transient mania after a cerebral hemorrhage, as it generally subsides spontaneously in a few weeks or months. At the same time it may blend into periodic depressive mania. Benon (*Revue de méd.*, July, 1911).

#### **Peripheral Disorders.—Contractures.**

—These may develop some weeks after the attack, and are usually spastic and functional rather than organic. They are associated with great increase of the tendon-reflexes. By a slow, steady counterpressure complete extension can be effected (mobile spasm), but the part quickly becomes flexed again on relaxation. This condition means little else than that the corresponding fibers of the pyramidal tract are involved. Separate from this is the early rigidity due to stimulation of the motor tracts by the irritative lesion.

**Edema.**—This condition of the paralyzed part is not of very frequent oc-

currence. It has been thought to be due to degeneration of the pyramidal tract, but it sometimes develops so early after the apoplectic seizure that the neural change could hardly have taken place. The amount of swelling may be little or much, and changes readily with the position of the patient. It collects at the most dependent part of the extremity.

*Neuritis.*—Occasionally a degenerative neuritis develops in the affected area. Considerable pain may be associated with it, though this must not be confused with the muscular tenderness that often follows directly on the paralysis. The reason for the occurrence of this form of neuritis is not well understood. Possibly it is an outside process grafted on such nerve-fibers as have least resistance.

*Decubitus.*—This is not, as a rule, as liable to occur or as resistant as in disorders directly involving the peripheral neurons. Still, from the inability of the paralyzed patient to relieve pressure on prominent parts, from the maceration by the discharges when not scrupulously cared for, and from the frequently impaired sensation, it is very easy for bed-sores to develop.

Trophic changes are supposed to be due to trouble with the innervation from the peripheral neurons; but Nothnagel and others have adduced some facts indicative of trophic influence from certain parts of the brain. Vasomotor disturbances, lowered arterial tension, etc., are observed on the paralyzed side. Some muscular shrinkage may be due to disuse, and more marked atrophy to neuritis.

#### DIFFERENTIAL DIAGNOSIS.

—This has to be made between hemorrhage and the following conditions: Embolism, thrombosis (including its

precedent conditions, such as syphilitic arteritis), pseudoseizures, certain toxemias (as uremia, gout, alcoholism, etc.), simple fainting, hysteria, and sudden death from various causes.

In the writer's experience the diagnosis of cerebral hemorrhage is not justified in cases of death occurring within five or ten minutes after the beginning of the attack. Details of 13 cases, with autopsies, in which life was prolonged for hours after the onset of the apoplectic attack, even when the hemorrhage was extensive, and had broken into the ventricles and filled them all, even the fourth. As a rule, extensive hemorrhage into the lateral ventricles is followed by a more rapid death than when the ventricles escape, but a moderate hemorrhagic exudate into the ventricles is not necessarily rapidly fatal. Even a large part of one cerebral hemisphere may be destroyed and the patient live for a considerable period, as was shown in one of his cases in which the hemorrhage destroyed the lenticular nucleus, a large part of the posterior limb of the internal capsule, and extended to the island of Reil, and, yet, the patient lived nearly two months. W. G. Spiller (Jour. Amer. Med. Assoc., Dec. 19, 1908).

The practice of uniting nearly all of these under the one head of apoplexy is, unfortunately, too common. While our diagnostic methods are not sufficient for all cases, the following principles will usually suffice to differentiate. Good medical judgment is here a strict necessity. To know our patients, their past histories, and any chronic disorders from which they may be suffering is of great advantage.

*Embolism.*—Against embolism speak: the absence of any distinct mitral or aortic lesion, the presence of headache or other prodromal manifestation; deep coma, especially late



development; vomiting, pronounced anisocoria, and advanced age.

**Thrombosis.**—Against thrombosis speak: youth unless the patient be a syphilitic, coincident or early rise of bodily temperature, early and deep coma, vomiting, great inequality of the pupils, high barometric pressure at time of onset, beginning of attack when the person is under effort or excitement, a pulse of high tension, the absence of prodromata, and the existence of vigorous general health.

**Pseudoseizures.**—The question of a pseudoattack can only arise where the subject is also suffering from either progressive dementia, tabes, disseminated sclerosis, or possibly the results of alcoholism.

The other possibilities can be excluded more readily and on general lines.

The points which differentiate hemorrhage in the brain from softening have been studied by the writer, on a basis of arteriosclerosis. Since 1900 about 422 patients with apoplexy have been treated at the public hospital and 256 succumbed. Of this number 201 came to autopsy, and in 5 both cerebral hemorrhage and softening were found. This leaves 197 cases for research on the differentiating points, as softening of the brain was observed in about a third and cerebral hemorrhage in the others.

After critically sifting and reviewing the various symptoms observed and comparing them with the post-mortem findings, he summarizes the signs that indicate cerebral hemorrhage as follows: Severe onset, especially with profound coma, and inability to move the limbs in the total and extensive cerebral paralysis, which frequently is rapidly fatal; blood-stained cerebrospinal fluid on lumbar puncture; age under 55 (especially under 50); low temperature at first, if no other cause for the sub-

normal temperature can be discovered; possibly a mild epileptic seizure as the initial symptom; retinal hemorrhage and rigidity of the paralyzed limbs, especially of the arms. Further useful signs, although of comparatively less importance, are hypertrophy of the heart without a valvular defect; albuminuria or nephritis, and normal or hyperemic papilla, and the vessels in the retina well-filled or gorged. There are no pathognomonic signs for acute softening, but the absence of initial loss of consciousness, with the serious paralysis and with the rarer partial, dissociated paralysis, suggest softening rather than cerebral hemorrhage.

Further useful signs are the incompleteness of the paralysis, pale papillæ, and undistended retinal vessels. Sometimes the paralysis comes on gradually, and there may be restlessness and vagueness. A valvular defect also points to softening, and likewise the determination of a prodrome or previous attack, or senile epilepsy. Low blood-pressure, if no other cause for it can be assigned, also points to softening; also clear cerebrospinal fluid. In the cases reported the hemorrhage was differentiated during life in 89 out of 108, and softening in 40 out of 63, the diagnosis being correct, therefore, in an average of 3 in every 4 cases. During the later series the data collected and recorded in this article enabled still more frequent accurate differentiation. A. Friedenreich (*Hospitalstidende*, vol. xlix, No. 47; *Jour. Amer. Med. Assoc.*, March 9, 1907).

**ETIOLOGY.**—The immediate cause of the hemorrhage is, of course, the rupture of some vessel, usually an artery, but occasionally a vein. Back of these vascular changes we come to the real causes that interest the practitioner. And here there is a broad distinction between senile conditions and those other factors that may be active at any period of life. In the young a consid-

erable proportion of the rare cases is due to the rupture of some single large aneurism in the vessels of the pia; as to their etiology, little is known. Very rarely in the newborn it occurs as part of a general hemorrhagic condition. Except for these and before the advent of senility we find either nephritis, syphilis, local softening, traumatism, abnormal blood conditions, or possibly certain nervous influences as the predominant causes. Because of similarity of conditions, in part hereditary, it is more common in some families.

Intracranial hemorrhage in the newborn studied in 23 cases. All proved fatal, except in five instances. The writer emphasizes the clinical importance of the location of the extravasation, above or below the tentorium, the hemorrhage having proved fatal in all his cases in which it was located below. The birth had been spontaneous and easy in more than one-fourth of the number, so that intracranial hemorrhage could not necessarily be ascribed to foreign intervention. It may evidently occur during normal delivery, especially hemorrhage over one hemisphere of the cerebrum. Scopolamine had been given to the mother in 1 of the cases. The constant screaming of the child, commencing about the second day, is an unfailing sign of hemorrhage causing painful distention of the dura. Seitz (*Münch. med. Woch.*, March 24, 1908).

Case of vasomotor hemiplegia in a boy of 10 who had mild cerebral apoplexy develop while exercising in a gymnasium. The hemiplegia was accompanied by severe pain in the opposite temple, but all the symptoms subsided without a trace after three days. Soucek (*Wiener klin. Woch.*, July 4, 1912).

While the after-history of but few of the cases of the so-called "curable" meningeal hemorrhage in the young is known, one in Cordier's experience suggests that the prognosis is graver

than is generally assumed. The first meningeal hemorrhage proved to be the subarachnoid localization of a toxi-infection. This probably is the condition in all such cases hitherto regarded as spontaneous and curable. There is probably always some meningo-encephalitis, but the brain is affected so slightly that the symptoms from this escape attention. Sooner or later, however, the latent toxi-infection may flare up and the point of least resistance in the brain give way. Cordier, Lévy and Nové-Josserand (*Ann. de Méd.*, Aug., 1915).

In traumatic cases the violence is a sufficient explanation. As a rule, the hemorrhage results promptly. But there are now many cases on record showing that several hours or days, even a week or more, may intervene. These are mostly meningeal forms, yet it is certain that some are intracerebral. It is these cases of delayed apoplexy that serve to associate the traumatic with the other varieties.

Case in which the internal carotid had been injured by a projectile and ligation of the external carotid was required later. Right hemiplegia and aphasia developed suddenly 4 days afterward, and in a few weeks there were epileptiform spasms on that side. The course of the projectile apparently exculpated the war wound as the direct cause of the brain symptoms. There was evidently some embolism in a cerebral artery and this in turn induced an inflammatory reaction in the surrounding tissues. Bastogi (*Riforma Medica*, June 8, 1918).

Nephritis is one of the most certain causes. The arteriosclerosis that develops may later degenerate, allowing the vascular tunics to give way. In any case the heightened blood-pressure (hypertrophy of left ventricle) and perhaps the circulating toxins so weaken the arterial wall that under some sudden stress it breaks.

Syphilitic alterations of the vascular pareties seem at times to be the immediate cause of their rupture; though this claim needs a better basis than the fact that the patient is a specific or that antisyphilitic remedies produce a good effect. Much more certain are the cases where the break results indirectly. In them a former specific arteritis, that may long since have run its course, has left behind it a cicatricial and hence weakened spot which ever after remains. Like all scar-tissue, this has less resistance and too often in time yields. This point has been strongly urged by Gowers. There are also evidently other cases in which softening of this origin makes the intermediary link to vascular rupture. In neither of these latter forms can specific treatment well have any value; they differ only etiologically from the general run.

Case of cerebral hemorrhage in a boy—a foundling—aged 10 years. At the age of 8 a suprapubic cystotomy was performed for a vesical calculus; at 9 he had a rheumatic facial paralysis, and later persistent headache leading to a diagnosis of chronic meningitis. Since the bladder operation he had had some cystitis, at times there being difficulty in urination. On the night in question he retired in his usual health, sleeping normally until near midnight, when he rose to void urine. Shortly afterward the noise he made in breathing awoke other children who slept in the same bed. He was unconscious and had a well-marked right-sided hemiplegia, the arm being in a state of semicontraction. On the left side there were clonic convulsive movements. The right upper eyelid was lower than the left; the pupil reacted to light, not to accommodation. There was no knee-jerk on the right side, but there was a Babinski; on the left the reverse state was noted. There was incontinence of feces and urine. The child never recovered

consciousness, and died on the fifth day. The autopsy showed a large hemorrhage in the left ventricle extending from the frontal to almost the occipital lobe. There was neither tumor nor tubercle; all other viscera were normal. The cerebral arteries were in a state of diffuse endarteritis. *Spirochaeta pallida*, in spite of close search, could not be found. The immediate cause of the hemorrhage was evidently the strain on urination, the blood-vessels being already diseased by a chronic degenerative process, probably luetic. G. Ghetti (Gaz. degli Ospedali, vol. xxx, p. 913, 1909).

*Local Softening.*—This may be due to traumatism, embolism, septic infection, syphilis, or whatever other cause. The focus is usually not a large one, and not the cause of any definite symptoms. Even if its presence were known, it is hard to see how anything could be done to remedy it or ward off this particular sequela. The prevention of the softening must depend on the treatment of the disorders that lead to it.

Abnormal constitutional blood conditions, such as scorbutus, purpura, pernicious anemia, leucocythemia, and severe infections with hemorrhagic diathesis, may act as efficient weakeners of the vessel pareties. Hemophilia is not known as a cause, however much it might darken a case.

All strenuous occupations favor the development of apoplexy, and sitting laborers, as shoemakers and especially tailors, seem prone to it.

*Nervous Influences.*—The probability of these as a factor was suggested by the writer to explain certain occasional peculiarities, as the onset during sleep, when the blood-pressure is lowest (though the possibility of exciting dreams can hardly be excluded); the absence of aneurisms as a source of hemorrhage in many cases, the asserted

occurrence of prodromata at times, and especially the occurrence of symmetrical hemorrhages. It is to the vasomotor control of these parts that such action must be assigned. This principle rests on the close bilateral association of the brain hemispheres, and presumes that any general influence—as from the abdominal or thoracic viscera, reaching some center or part of one hemisphere—affects at the same time or in immediate sequence its opposite in like manner. Possibly by allowing a dilatation of the arteries to the respective parts a strain is exerted on the vessels secondary thereto, and thus weak points give way. Whether this cause can of itself be sufficient or whether it at most is only an immediate cause cannot be stated.

*Senility.*—It is supposed that the senile involutionary shrinkage of the brain tends to a decrease of the normal counterpressure of surrounding structures on the arterial wall, and thus favors a so-called *ex-vacuo* form. The changes that old age brings are universally recognized as predisposing to apoplexy. This has, in times past, led to the assumption that cerebral hemorrhage was only a matter of years. Because senility is added to the other factors this trouble is more frequent in the aged, though it has been found that in the very old cerebral thrombosis is a more frequent result. Mix (1906) finds that "cerebral hemorrhage becomes more and more likely in old people up to the age of 72." But, as the previous causes are quite as common in the younger or stress years of life, there is no immunity at any period.

Distinct from the above are the immediate provoking causes, of which there are many: overexertion, as straining at stool, lifting of heavy weights;

walking uphill and against wind, stunts; plethoric states, as after excessive eating; rage, fright, or other sudden, great emotion; the sexual act or other excitement, severe coughing, meteorological conditions (rise in barometer, fall in atmospheric temperature), surface chilling, etc., come under this head. These all act by increasing the blood-pressure. Presumably they are, of themselves, insufficient without previous vascular change.

The following are grounds for predisposition to cerebral hemorrhage, as some families exhibit such a predisposition, but this is usually an indirect result of inherited tendency to arterial degeneration: 1. From the history of a previous attack. 2. From the constitutional state which induces arterial degeneration, *i.e.*, senility, chronic nephritis, rheumatism, gout, diabetes, syphilis, lead poisoning, etc. 3. From the presence of arterial degeneration itself, as manifested in the radial and temporal arteries by their rigidity and tortuosity. This evidence of arteriosclerosis is extremely suggestive, but is not positive proof of a similar condition of the cerebral vessels. It has recently been stated that tortuosity and prominence of the temporal arteries are commonly due to the frequent pressure of a rigid hat-band. As a matter of fact, however, many cases are on record in which post-mortem examination and careful microscopic investigation have shown normal cerebral vessels coexisting with degenerated temporal and radial arteries. The presence of retinal hemorrhages and ophthalmoscopic evidence of arteriosclerosis furnish indications of considerable value. They are extremely significant, inasmuch as they point to a state in which cerebral hemorrhage is most likely to occur. 4. From the presence of continuous high blood-pressure (as determined by the radial pulse and the sphygmomanom-

eter), chronic interstitial nephritis, and ventricular hypertrophy. These are matters which demand painstaking investigation. Leszynsky (*Med. Record*, Feb. 27, 1909).

From the standpoint of accident insurance, the real cause of an apoplectic stroke is either a disease of the arteries, resulting in a cerebral hemorrhage, or a disease of the heart, resulting in a cerebral embolism. In either case some accident may be the exciting cause, or at least play a significant rôle in the occurrence. In cerebral hemorrhage the breaking of the weakened vessel may be caused by undue exertion, by abrupt change in temperature of the body, by the rise of blood-pressure following fright. Of course, concussion of the skull and brain may have a similar effect. Procházka (*Med. Blätter*, Nov. 4, 1911).

Cerebral hemorrhage of the newborn, a common condition, is due to trauma in normal or rapid deliveries, to congestion or asphyxiation in slow deliveries, or to disease of the child itself. The so-called hemorrhagic disease of the newborn the writer considers a much neglected but very important cause. Forceps deliveries, advanced age of the primipara mother, and syphilis probably do not play as important a rôle in the etiology of this condition as was formerly supposed. Margaret Warwick (*Amer. Jour. Med. Sci.*, July, 1919).

**PATHOLOGY.**—This resolves itself into three questions: (1) as to the vascular changes preceding or attending the rupture, (2) as to the blood thrown out, and (3) as to the changes of nerve-tissue resulting therefrom.

1. In the usual spontaneous cases there is always some alteration of the vessel walls that weakens their resistance.

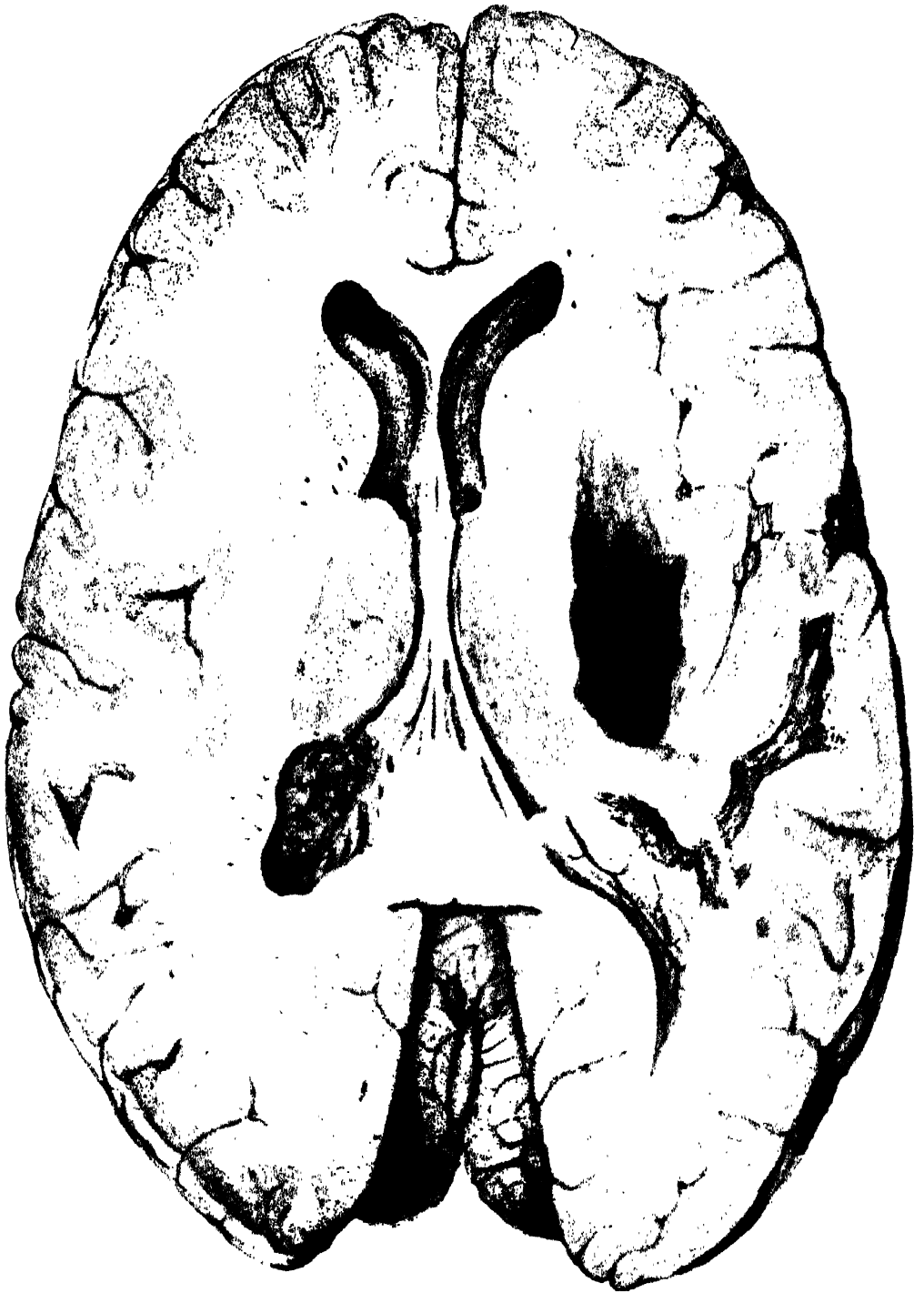
Fatty and atheromatous degeneration is common in aged subjects, and appears earlier in those who have done heavy lifting, overindulged in alcoholics,

or for any cause developed premature senility. Nephritis and the uric acid diathesis lead to arteriofibrosis, which later breaks down. Specific arteritis leaves an atrophic condition of the vascular wall, and this may, in time, yield. Aneurisms (miliary) sometimes develop, as found by Bouchard and Charcot, doubtless on the basis of some of the conditions just mentioned or from hyaline degeneration of the walls of the smaller arteries, and presently one or the other of these may give way. Later studies have shown that far from all spontaneous cases are due to the rupture of such aneurisms. We must conclude that weakened spots sometimes give way directly, *i.e.*, without the intervention of such dilatation.

In numerous other cases purely local troubles so undermine the vessel's strength that it ruptures. The writer has shown this for foci of softening; these erode and weaken the wall of some vessel in the involved area; then, of course, rupture easily results. Embolism also, and in like manner, sometimes occasions an early break at the point of plugging. Then tumors not rarely so weaken and drag on the local vessels that small and large hemorrhages result.

Though any part of the brain may be the site, there are certain favorite starting-points. These correspond to the territory of the terminal arteries, *viz.*: the pre- and post-perforating and the branches from the basilar entering the pons. Statistics regarding site have been collected in this country by Dana.

Series of cases of intracranial hemorrhage due doubtless to laceration of the tentorium, to which occurrence Beneke has recently called attention. But the writer describes a number of other cases in which the hemorrhage occurred at other points



Recent and Old Lesions of Cerebral Hemorrhage in the same Brain.



and the tentorium was intact or could not be incriminated in the bleeding. When the skull is frozen for pathological examination, there are a number of minute extravasations of blood around the medulla oblongata. There may be no symptoms for several days, but then sudden cyanosis and dyspnea develop and the child succumbs in a few days at most. The cases of tardy asphyxia in newly born infants are generally referable to these minute hemorrhages when no other cause is apparent.

The writer also found retinal hemorrhage in 50 per cent. of the infants born from a contracted pelvis, in 40 per cent. of the prematurely born, and in 20 per cent. with normal delivery and a medium-sized child among 200 newly born infants he examined in 1900. Others have reported similar findings, and traces of hemorrhage in other organs, the liver, adrenals, and serous membranes, are common in children born asphyxiated. On the other hand, laceration of the tentorium does not always mean that hemorrhage has occurred. L. Seitz (Zentralbl. f. Gynäk., Jan. 6, 1912).

Out of 128 cases of intracerebral hemorrhage analyzed by the writer, in 24 (about 18 per cent.) the brain showed discrete multiple hemorrhages, none of them being traumatic. Plurality of hemorrhages was represented in 3 brains by three distinct sites of hemorrhage, and in the remaining 22 by 2. The combination of 1 hemorrhage into the internal capsule or basal ganglia and 1 into the pons was most frequent, occurring in 15 brains (63 per cent.). Of the 7 brains (32 per cent.) in which both hemorrhages were into the cerebral hemispheres, 5 presented bilateral symmetrical hemorrhages implicating both internal capsules or basal ganglia. Greenacre (Bull. Johns Hopkins Hosp., Feb., 1917).

2. As to the blood thrown out. There is less resistance to the outflow in the

gray than in the white matter. It may vary in quantity from minute capillary extravasations up to those of several ounces. Some coagulation soon takes place in the extravasated blood; but before this has occurred the blood—if, *e.g.*, it has found a way into the cavities or meninges—may have scattered widely in these spaces and have even passed over in part to the other side. Where, however, it has not broken through, but been retained in one focus, it remains long enough and sufficiently fluid to work its way into all accessible interstices. This is assisted, so long as the flow continues, by the pressure of the blood in the ruptured vessel. As a consequence, the focus is always irregular and ragged in shape. Much also depends on the surrounding structures; if these are stratified tracts the blood naturally makes a long pocket; if, however, these are soft tissues or matted fibers a more globular focus results.

The free fluid and granular material are gradually absorbed, leaving the characteristic brownish pigment and sometimes pultaceous material as a cyst.

In the case of a child, 1 year old, a puzzling clinical picture was explained by hemorrhage in the right hemisphere of the brain. There was no sign of leukemia, but chronic nephritis had evidently injured the vessels in the brain as rupture had occurred. Recent research by Riva-Rocci has shown the great fragility of the vascular walls in children. Conti (Pediatrics, Feb. 15, 1921).

3. Changes of nerve-tissue, caused or provoked by the hemorrhage. The primary effects are tearing and compression. The fibers and gray matter may be forced apart, but often they are ground up, disintegrated, and mixed with the blood, making a pulp into which project abundant fragments of severed tracts. Where fibers are simply forced



apart, there may be scarcely any of this chowdering, the compression of adjacent tissues being then all the greater. In limited effusions the compression is exerted chiefly on the immediate neighborhood; but, where the volume is considerable, it may affect the whole brain, as is shown by the vomiting, coma, etc.

Nerve-fibers, once severed, do not, so far as we know, ever reunite; consequently loss of function due to this cause must be permanent. On the other hand, fibers whose function is disturbed by compression or edema *may* yet regain their usefulness, and to this is due the degree of recovery that we often see. For on this acute stage there follows one of reaction. It is largely due to the accompanying infiltration and inflammatory edema of adjacent parts that so many cases end fatally in from two to ten days. Even where life is retained this reaction still further jeopardizes neighboring structures and diminishes the extent of eventual recovery.

There are, finally, certain secondary changes of nerve-tissue that may develop. These affect only such nerve-fibers as have either been directly severed by the effusion or so much involved as to be unable to recover even their trophic function. Then the portions of these neurons that have been cut off from their respective cells undergo degeneration the same as do severed fibers in peripheral nerves. In the case of the pyramidal or spinal motor tracts this degeneration may extend down the cord to the anterior horns; but the terminal, or spinal, motor neurons, being independent structures, are not generally involved in this process. Of course, fibers going to other parts of the brain will degenerate in

like manner if severed from their parent-cells. While in the peripheral nervous system there may be a regeneration of severed or degenerated fibers, nothing of the kind is known to occur in the central nervous system.

**PROGNOSIS.**—This must be based on the following factors and on the accuracy with which we can determine them. There are, however, two separate questions in the matter of prognosis: one has regard to the continuation of life and the other to the extent of recovery from the attack.

*The Age of the Patient.*—In childhood the rare cases that do occur are usually severe; but, if the attack itself is outlived, the natural recuperative power is so great that the person will live on indefinitely. Improvement may be expected for some years, but entire recovery is unusual.

In middle life the outcome depends on the causal trouble and the severity of the apoplectic attack. Where the motor involvement is not great or is due to indirect pressure absorption of the clot permits a practically complete restitution of all functions. More often some impairment of the involved area remains. If the primary cause still obtains, this also interferes with recovery and the general outlook.

In senile conditions (tortuous or calcified arteries, dry and wrinkled skin, arcus senilis, etc.) but limited recovery is to be expected. Life may be prolonged, but most depends on the promptness with which the attack is checked. The subsequent length of life depends much on the kindness and care with which the chronic invalid is surrounded.

*Nephritis.*—Here we must distinguish between unimportant secondary or casual albuminuria and real kidney disease. The latter, when present,

limits recovery and determines the eventual duration of life. Even with this complication, however, if the site and extent of the effusion be favorable, the paralytic condition may be fully recovered from.

*Syphilis.*—The existence of this systemic infection is principally of etiological importance. It may constitute an indication for treatment, but otherwise has little significance.

*Severity and Nature of the Attack.*—This is the great guide to prognosis.

Coma, stertor, vomiting, prolonged semiconsciousness, extensive and complete paralysis, etc., indicate a large effusion with much damage to the brain, both in local destruction and general shock. Consequently there is immediate danger to life and much less chance of functional recovery when life is prolonged. In proportion as these features are less prominent the chances for preservation of life and for recovery are increased.

Prolonged high temperature, or a rise to 104° or 106° F., makes a fatal prognosis probable. Especially about the fourth to sixth day a rise in bodily temperature, deepening of coma, increased muscular relaxation, and the advent of Cheyne-Stokes breathing presage approaching dissolution.

General convulsions, as indicative of ventricular rupture (barring uremia), are a particularly bad omen, death usually resulting in from a few hours to a few days.

*Location and Size of the Lesion.*—These two features are complementary. For, though much depends on the site, a large outpour by its mere volume may include temporarily all the effects of the smaller, and certain general effects in addition.

Pontile hemorrhages are more often

promptly fatal, doubtless from the importance of the local centers and passing tracts. The outpour is also more rapid because from relatively large vessels and close to the parent-trunk. On the contrary, hemorrhages of the pallium (that part of the cerebral hemisphere above the central ganglia) commonly become vast in size before inducing as serious symptoms. Cerebellar apoplexy may be lethal from pressure on the respiratory and adjacent centers.

Inequality of the pupils developing as a part of the attack, especially where the larger is on the side of the supposed hemorrhage, suggests a large focus, and hence points to a more serious condition. But this is indecisive by itself.

After the acute stage has been tided over, the extent of presumable recovery is the main matter for prognosis. Here, besides the points already presented, other manifestations have to be considered. The state of the tendon-reflexes in the involved area must be determined; if there is any increase compared with the other side, we can pretty safely conclude that some permanent injury of nerve-tracts will remain, though a slight local increase is not incompatible with apparent functional recovery. Any marked increase of these reflexes—as ankle-clonus or wrist-clonus or a knee-jerk of ten inches, say—means lasting paralysis. The occurrence of edema or contractures in the paralyzed part signifies so grave a lesion of the motor path as to preclude hope of full recovery.

The anesthetics that are so frequently present in the early or acute stage rarely prove lasting. The occasional development of chorea in the affected extremities is in so far a good sign as it indicates returning conductivity of the motor tracts.

**TREATMENT.**—It cannot be too strongly urged that the first *desideratum* is a correct diagnosis. Upon this must our treatment primarily depend to be efficacious, since the affections that most closely simulate cerebral hemorrhage demand directly opposite treatment.

The writer emphasizes the necessity of taking into consideration the conditions that conduce to cerebral hemorrhage, namely, renal, circulatory, and arterial disease. The most important of these is the blood-pressure. In the light of recent research the most active agents in raising and maintaining high blood-pressure are the derivatives of tyrosin. Hence the great necessity for avoiding foods which contain these substances in excess. Chief among these are meat, eggs, and milk. E. M. Hummell (Med. Record, Dec. 2, 1911).

As the therapeutic indications in cerebral hemorrhage vary considerably according to the stage of the trouble, they can best be considered under the following heads:—

**Prevention.**—In general, the prophylactic management is indicated by the etiological factors. If there are any suspicions of prodromata, the patient must be warned against all lifting and straining, the bowels be kept free (calomel or salines), any overtension of the pulse be eased by mild depressants, and the patient kept in a warm atmosphere well protected from all chilling. Digitalis and cardiac stimulants of every sort should be carefully avoided. Any nervous overtension can advantageously be remedied with **bromides**, and their use here is regularly in order. **Gelatin foods** are also recommended to favor coagulation.

Why have the arteries burst in apoplexy when the kidneys are healthy? The arteries may be the seat of atheroma or sclerosis; but although diseased, they have not be-

come calcified, as in cases of Bright's disease, but they have ruptured nevertheless. The reason of the giving way of the arteries is their subjection not only to the mean pressure of age, but further to the mean pressure of a reluctant peripheral circulation. They have given way in consequence of the accumulation of obscure stresses which might be averted. The cause of the obstruction must be either a narrowing of the caliber of the arteries or a very extensive area, or else an increased viscosity, with excessive friction, of the blood itself. If, as regards the mechanism of persistent rise of the arterial tension, we are in the dark, there is fortunately less doubt as to the treatment of the condition. If a patient is to be saved from apoplexy, this can only be effected by long anticipation. A tendency to hypertension seems to run in families; if this is so, then it is most important that vigilance be exerted, especially as regards members of such families. But the condition is so widespread that it cannot be regarded as confined within such narrow limits. It is not rarely met with even in children and young people. In them the arteries may be thickened, but the change affects the muscular coat and not the intima, and this hypertrophy may disappear just as a hypertrophy of the heart disappears when the causes of exceptional strain are put on one side. Arteriosclerosis as distinguished from the sclerotic decay of senile involution is not the cause, but the result, of rising arterial pressure. Hence prevention consists in the detection of a special tendency to a persistent mean rise of pressure. Every adult of 40 and upward should have his blood-pressure measured. Clifford Allbutt (Bristol Medico-chir. Jour., March, 1905).

Since food has become scanty and dear, the writer has not seen as many male cases of cerebral hemorrhage as previously, but conversely, the cases of softening of the brain have increased fourfold. During 7 years he

had in his service 46 of the latter and 38 cases of cerebral hemorrhage, while for the first 4 years the totals were only 14 to 21. Salomonson (Nederlandsch Tijdsch. v. Geneeskunde, May 31, 1919).

*During the Attack.*—Some cases are promptly fatal, meningeal and ventricular forms being usually of this kind. Nearly always, however, the effusion progresses for some time. It is here that the physician can be of great service, and as there is rarely time to call for consultants it is important that every practitioner understand the methods fully.

The first and main object is to stop further hemorrhage. *Our efforts should be directed to a lowering of the arterial pressure, and to a derivation of the blood-current to other parts, i.e., in general, to a reduction of the supply to the brain.* For this purpose a variety of means are available and when promptly applied are successful.

*Position of the Patient.*—The main essential is a sufficiently prone position to insure complete relaxation of all the muscles, since we know that muscular effort tends to increase arterial tension. On the other hand, dropping the head too low favors the flow of the blood to the brain: a principle that we apply in cases of fainting, anemic exhaustion, chloroform syncope, etc. The best position, then, for a patient with progressing cerebral hemorrhage is to have the body sufficiently reclining to be fully relaxed and the head considerably elevated.

Absolute quiet is insisted upon by the writer, in cases of apoplexy. The patient must not make a movement or speak. His clothes should be cut off, and he should be placed in a cool room as near as possible to the place of seizure, with his head and

chest slightly raised. An **ice-bag** should be placed to the affected side of the head if there is any facial congestion. Nothing can be done if vomiting occurs, except to wipe out the mouth and keep the head and tongue forward. Mustard pastes, etc., are useless. **Venesection** is indicated where the diagnosis is certain and the full bounding pulse persists while the coma continues or grows worse. It is more effective when done early. He withdraws 200 to 300 c.c. (6½ to 10 ounces) of blood from the arm on the unparalyzed side. A small, weak, rapid pulse with pallor contraindicates it. Collapse, convulsions, insomnia, and headache are treated symptomatically, often with **opiates**. If there is complete unconsciousness, nothing should be given by the mouth; if the food-pressure drops from inanition, so much the better. Feeding should be done with the stomach tube only when paralysis of the muscles of swallowing persists with complete consciousness. If coma continues, **rectal feeding** should be used. Straining at stool is dangerous, but cautiously given enemas may be useful. The after-effects, contractures, etc., must be treated according to the situation and severity. If the hemiplegia develops gradually, as in arteriosclerosis, the **iodine** should be started at once; but if the patients are unaccustomed to the drug, it is better to wait at least a week after the seizure. Goldscheider (Deut. med. Woch., Nov. 28, 1907; Boston Med. and Surg. Jour., Feb. 6, 1908).

Sometimes the vomiting in such a case appears to be eased by turning the person on the right side; it is further claimed that turning the person on the paralyzed side eases the stertor.

*Vasodrugs.*—The proper use of these remedies is our most valuable single resource. Ergot can well be discarded. Adrenalin, digitalis, etc., are contraindicated. All stimulants, vascular tonics, morphine or opiates, and, for the time,

strychnine should be carefully avoided. The cardiovascular depressants—**gelsemium**, **veratrum**, or **aconite**—are sufficiently powerful and yet ordinarily safe drugs. Either of these can be administered hypodermically, though they also act promptly by the mouth. Where the pulse warrants its use (and here accurate determination of the pressure is our best guide), it is well to begin with **gelsemium**. In adults the fluidextract can be started with an initial dose of 10 drops (0.6 c.c.) and followed by 5-drop (0.3 c.c.) doses at intervals dependent on the closeness with which the case can be watched.

More active, however, is the preparation **gelsemin** in doses of  $\frac{1}{10}$  grain (0.0065 Gm.) or less. It should be pushed until its physiological action is manifest, whether little or much is required. The full benefit of the drug is not obtained unless its paralyzing effect is secured.

One of the most commonly used agents is **nitroglycerin**. And its employment can be defended on the double ground of its quick action and its effect (in doses of  $\frac{1}{50}$  grain—0.0013 Gm.) of materially lowering the general arterial pressure. Its transient character is a drawback, though this can be met by frequent dosage. It reduces pressure, however, by dilatation of the arteries, and this, unfortunately, may serve to increase the outflow. Where no other means is at hand, it may be justifiable to use it. My observation of its effect in these cases has not been gratifying. It is more rational to resort to the group that directly depresses the arterial force without dilatation. And my own clinical experience has long corroborated their superiority.

Of course, the hypodermic method is here specially in place. The work of Tilney and Brockway (1907) shows that a moderate effect, beginning in a few minutes and reaching its maximum in about thirty-five, can be secured by hypodermic injection of  $\frac{1}{50}$  grain (0.0013 Gm.) of crystal potent **aconitine**, and that an equal, but quicker result (maximum in twenty minutes) can be gained by like use of  $\frac{1}{5}$  grain (0.013 Gm.) of **gelseminine hydrochloride**. The usual hypodermic tablets of aconitine "pure crystal" up to  $\frac{1}{20}$  grain (0.0005 Gm.) had, however, the opposite effect (raised the pressure!), and are worse than worthless for this purpose. Consequently, for successful use hypodermically the utmost care must be taken to get just what is needed.

When medication on this line has to be continued for any length of time, it may be necessary to change, especially from full doses of gelsemium. Then the **nitrites** become useful. It is usually advisable to keep up some influence of this kind for from a couple of days to a week.

*Autodepletion.*—This can be practised by **constriction of the extremities near the trunk**. This is a very promptly acting, but temporary expedient with many limitations. A coarse binder should be used. Brittle vessel walls are a distinct contraindication. Only sufficient force should be used to more or less shut off the veins without affecting the arteries (if too much we but strangle the extremity; if too little we fail of our purpose). Care must be had, lest the extremity become too cold. Finally, the constriction must be eased up gradually, lest the sudden influx into the general circulation again start up hemorrhage.

**Warm bottles to the extremities, mustard to the soles, and gentle frictions** are, of themselves, useful in drawing blood to the parts, and are doubly so when constriction is resorted to.

Compression of the carotids is a doubtful measure, as the vessels in older patients are easily injured and a steady control of the current for any length of time is rarely possible. Ligation of a carotid is literally adding injury to insult.

**Ice to the head** is a popular plan, but also of very uncertain value. If used at all for this purpose, it might far better be applied over the **carotids in the neck**.

*Depletion of Body Fluids.*—Formerly this was the main treatment, and practised in the form of **venesection**. Many still think highly of this procedure for vigorous patients with a tense pulse. "The indications for venesection are a regular, strongly acting heart and an incompressible pulse." The abstraction of but a fraction of an ounce will sometimes accomplish the purpose. Closely to this measure, but sometimes very effective, are **puncture of the brain**, and also **lumbar puncture**, the loss of cerebrospinal fluid in the latter case reducing markedly cerebral pressure.

The most common and still accepted method is by purgatives, as a drop of **croton oil** on the tongue, a good dose of **calomel**, or a **glycerin and sulphate of soda enema**.

Case in which **puncture of the brain** and **lumbar puncture** were resorted to for intracranial hemorrhage. The patient was still unconscious two hours after a fall on the head; the breathing was stertorous, the pulse 64, while a small hematoma was evident in the right orbit and temple.

The next half-hour the pulse dropped to 48 and the patient seemed moribund. A Neisser-Pollack puncture was then made back of the right Krönlein point, and 8 or 10 c.c. (130 or 162 minims) of black blood released. The breathing ceased to be stertorous at once and the pulse increased to 68; the condition improved rapidly to such an extent that osteoplastic trephining became possible; 35 c.c. (1¼ ounces) of blood were evacuated from the hematoma, and recovery was soon complete. In another case three punctures revealed multiple hematomas, the patient improving wonderfully while 70 c.c. (2½ ounces) of fluid were being evacuated from the right posterior Krönlein point, opening his eyes and asking questions during the operation. Hesse (Archiv f. klin. Chir., Bd. xciii, Nu. 1, 1910).

Case of meningeal hemorrhage in a boy aged 10 who came into the clinic comatose, with complete left hemiplegia, left arm strongly contracted, and left lower extremity difficult to extend; foot in equinovarus. The attack was sudden and occurred immediately after a bath; the child cried for ten minutes, then became unconscious and convulsive, with nystagmus and vomiting. There was paralysis of the right third nerve, with partial ptosis, elevation of the eyebrow, slight external strabismus; no mydriasis; pupils contracted and feebly reactive to light; left lateral hemianopsia. A series of **lumbar punctures** brought about rapid improvement. This child was previously healthy, no tuberculosis or syphilis; no albumin in urine. It was found that about a fortnight previous to the attack the child had fallen on the back of his head while skating. The diagnosis was meningeal subarachnoid hemorrhage. D'Espine (Presse méd., May 17, 1911).

There may be other matters that require attention. Convulsions should be promptly stopped, and for this purpose

a few whiffs of **chloroform** may suffice. The danger of false swallowing (or inhalation of material) increases with the loss of reactivity. The efforts of vomiting are injurious.

A gouty state is common, and generally presumable, because senility of the organs generally justifies some **lithia** or **potash**, combined with a **diuretic**, **nitrous ether** and **spirit of juniper**, to which some **digitalis** may be added—more if thrombosis is suspected than if hemorrhage is probable. The opposite rule should obtain with an aperient. If a clot has formed, only gentle action of the bowels should be secured; if a vessel has ruptured, an active purge is wise, such as **croton oil**, to lower the blood-pressure. Salines, it should be remembered, seldom alone act well in the horizontal posture; they need the aid of gravitation. Blood should be drawn to the extremities.

If there is reason to regard the lesion as thrombosis, little more can be wisely done. We have no practical agent to reduce the coagulability of the blood. **Citric acid** is said to have this effect, and may be given as **lemon juice** in plenty of water. When hemorrhage may be confidently diagnosed, the treatment should be such as to increase the tendency of the blood to clot. **Salts of calcium** have this effect, and may be given in whatever form can be most promptly obtained. If the **lactate** or **chloride** is not at hand, common **chalk** may be converted to a soluble salt by any suitable acid that is available. **Arsenic**, by hypodermic injection, has a similar effect, and  $\frac{1}{2}$  grain (0.013 Gm.) of the **arsenate of sodium** may be given in a few drops of water. There is no reason to believe that small doses of iodide of potassium, which are constantly given at the early or later stage, exert the slightest influence.

But one measure is imperative in every case of either kind—physical tranquillity. It should surely be superfluous even to mention this, but

experience shows, too often, that it still needs to be insisted on. Even in the slightest case, if the patient must be moved, it should be as little as possible, and he should be absolutely passive. Gowers (Brit. Med. Jour., July 6, 1907).

In thrombotic apoplexy the author obtained excellent results through early reduction of the viscosity of the blood by means of **citric acid**. H. B. Hemenway (Jour. Amer. Med. Assoc., April 6, 1912).

If the bladder is full, **catheterization** may be necessary.

*Avoidance of Relapses.*—In many cases the immediate onset is followed by an evident tendency to cessation of the outflow. Shock and other manifestations subside. This early lull seems to have escaped particular notice, but in many cases, especially that eventually become severe, such a history can be obtained. It is all-important that this be taken advantage of. Too often the patient or attendant thinks lightly of what has so easily subsided, some degree of activity is resumed, and then in a few minutes or an hour or more comes the fuller seizure with its lasting injury. Complete quiet, active and passive, mental and physical, is the radical indication, with prompt recourse to the depressant sedatives.

*Treatment of the Reaction (or the Subacute Stage).*—Here there are still some shock, an actual destruction of brain-tissue, a compression of adjacent tracts by the extravasation, and an inflammatory reaction of immediately surrounding parts. We have little to offset this. Counterirritation can hardly act that deeply. **Iodides**, to favor quick absorption of clot, are the routine treatment.

**Trephining**, with evulsion of clots, would be in order in this condition, although, owing to difficulty in exact

localization and the usual depth of the focus below the surface, such operative relief is not always feasible. Surgical measures are increasingly being resorted to however, often successfully.

The writer has resorted to **trepthing** for intracranial hemorrhage in the newborn four times, with two successes. At the onset the indications for immediate surgical intervention are as definite in many of these cases as they are when corresponding symptoms are unmistakably the result of a traumatic hemorrhage occurring in adult life. A more careful study of the symptomatology of these cases is necessary, so that the condition may be recognized earlier and immediate operation may be undertaken for their relief, and possibly to ward off the consequences of the hemorrhage, such as spastic paraplegia, diplegia, epilepsy, amentia, etc. With proper regard for hemostasis and careful avoidance of exposure, a newborn child will stand a cranial operation well. If it can be demonstrated that a craniotomy on the newborn child, when conducted with due precaution and delicacy of manipulation, is comparatively free from danger, the immediate risk of death and the sorry late consequences of meningeal birth hemorrhages may be avoided in many cases by surgical interference. H. Cushing (Amer. Jour. Med. Sci., Oct., 1905).

Case of fissure fracture of the skull without depression of bone or signs of compression, causing a supradural hemorrhage from the middle meningeal artery and total right hemiplegia. The left facial nerve was apparently somewhat involved by the extension of the clot. The removal and cleansing out of the clot relieved the hemiplegia, though the muscles were still slightly weaker for about five days.

The patient was at work at his trade, that of a brick-layer, a week after his discharge from the hospital. L. L. Smith (Jour. Amer. Med. Assoc., Oct. 8, 1910).

Case of cerebral hemorrhage in the newborn in which the delivery had been a breech presentation. The next day the infant showed a paralysis of the left arm and a slight facial on the same side. The anterior fontanelle was tense and bulging. A diagnosis of intracranial hemorrhage was made. At operation a large horseshoe flap on the right side was made to include the parietal bone. This flap was turned down. On exposing the anterior fontanelle, hemorrhage on either side could be demonstrated through the dura. The parietal bone in part was severed and turned down as an osteoplastic flap. On opening the dura the blood spurted out under pressure. The whole right hemisphere was irrigated. While the relief of tension had been marked, there was still considerable bulging of the brain substance. The anterior fontanelle to the left of the median line was then opened for about an inch, when some blood was discharged, bringing the intracranial tension almost to normal. The dura and bone flap were roughly sutured into position. Two weeks later the child was discharged from the hospital apparently well, but some few weeks later died of a gastroenteritis. The cerebral condition was found normal *post mortem*. J. R. Torbert (Arch. of Ped., May, 1910).

The writer recommends **trepthing** in case of cerebral hemorrhages. To sit idly by and leave a brain scar or unabsorbed cyst to make the patient aphasic or hemiplegic for life is unwarranted. In a case of intestinal perforation or rupture of tubal pregnancy, prompt surgery would be the rule. Surgery of the brain is equally imperative, though not necessarily so urgent. In hematoma of the brain the first seventy-two hours are likely to settle the fate of the apoplectic, providing he survives the shock, and after that the patient is generally in better condition for operation than in the usual case of cerebral traumatism. Each day thereafter for a limited time, say ten days from the



attack, it is still more favorable, and the surgeon can choose his time for operating. As technique improves and the time to operate becomes more definitely known, the percentage of fatal cases will become less. Reports of a case operated on eleven days after the attack with good results, the patient being occupied as a freight conductor when last seen, twenty-two months after operation. J. D. Milligan (*Jour. Amer. Med. Assoc.*, June 17, 1911).

Two cases of subdural hemorrhage in the newborn relieved by the simple operation of incision through the coronal suture and allowing the blood to escape. One case was bilateral, the other unilateral. The earlier case is now over a year old and seems perfectly normal in every respect. The other case was but recently operated upon. The credit for the operation belongs to Cushing, but his osteoplastic flap is hardly necessary in these tiny infants. They usually die shortly after birth, or, if they live, epilepsy and spastic paralyses are likely to develop. The symptoms are simply those of cerebral pressure: the child is irritable, does not nurse, is pale and sickly. The respirations become shallow, the pulse rapid and full, and cyanosis may develop. There is no pulsation in the tense fontanelles. The blood comes usually from one of the large veins of the cerebral cortex. C. Simmons (*Boston Med. and Surg. Jour.*, Jan., 1912).

Case of emergency surgery with inadequate instruments performed in the Adirondack woods. The patient was a physician who had received a blow on the head, and shortly afterward presented evidences of extradural hemorrhage. The only instruments that the author could secure for making an opening in the skull were a small antiquated trephine with several teeth gone, a small gouge, and a carpenter's hammer. The trephine proved worthless; so the operator was compelled to chisel out the bone over the selected area. A collection of fluid blood estimated at

about a small cupful was exposed and evacuated. There was discovered a wound in the posterior branch of the middle meningeal artery. As soon as the blood escaped, the brain began to pulsate normally and the congestion diminished. A small drain of plain gauze was inserted to prevent further hemorrhage, and the wound was closed down to the brain. The patient made an uninterrupted recovery. B. T. Tilton (*N. Y. Med. Jour.*, Feb. 24, 1912).

Case of a man, who, after an automobile accident, was unconscious for several hours and then seemed to have suffered little for a period of nearly 2 months. A button of bone was removed from the front of the middle of the right motor area and dura was incised. The patient recovered from a first operation, a large quantity of dark colored fluid having escaped, but his condition was not improved. At a second operation a large osteoplastic flap was turned down in the right frontoparietal region. On incision of the dura the cortex was found to be covered by an organized blood clot 0.5 cm. in thickness, which had evidently compressed the parietal and frontal lobes. The case is recorded not only because of the unusually satisfactory operative results, but also because the mental symptoms were evidently the result of the involvement of the frontal lobe. None of those who witnessed the operation had ever seen so large a clot removed from a living subject. C. A. Elsberg (*N. Y. Med. Jour.*, Sept. 30, 1916).

During this, the reaction, period we may have to continue depressants and wait, with *nux vomica* or its alkaloids. "Negatively the use of digitalis in a patient who has once suffered from brain hemorrhage is ever after a risky matter."

For the hemiplegic after the condition has settled down into the chronic stage our resources have been somewhat limited. **Strychnine** or its con-

geners internally, sometimes **electricity** locally to the muscles, and care of the general health comprise all that is rational in customary procedure.

We can now make a better showing. Twenty years ago at the Kings County Hospital the hemiplegics were in large part a bed-ridden and deeply demented class. Now they are soon trained to sit up and if possible get about and be mildly active. At the present time, out of 43 patients of this class only 1 is confined to bed. And this does not include the many who have improved sufficiently to go home or to the infirmary, but only the accumulated worst cases plus a few fresh arrivals. The stuporous dementia is to an extent a secondary and avoidable condition. Their own lives, as well as those of the attendants, are far more tolerable. Everything should be done to stimulate activity in the impaired nerve-tracts. The patients are roused, lifted—if not too feeble—into a sitting position, interested once more in life. By exercising actively and semipassively the paretic parts, we can save the patient from the further degeneration that so often ensues and may even effect great gain. Ere beginning this plan, however, we must wait until the danger of immediate relapse is past, say, usually until the end of the first week or ten days.

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**CEREBRAL PARALYSES OF CHILDREN. — DEFINITION. —** Children may present at an early age many of the forms of organic cerebral diseases observed in adults, and originating under analogous circumstances from similar causes. But under the term “cerebral paralyses of children” are understood morbid condi-

tions which present special clinical pictures, and which commence at a period of life when the brain and its commissural and projection fibers are not entirely formed. They may, therefore, develop in intra-uterine life, or very shortly after birth, or during birth. They are, speaking generally, the result of a chronic inflammation of the brain, and this inflammation (encephalitis) may occur either *in utero* or outside of the uterus following a trauma, a hemorrhage, or softening from any cause. The result is cerebral sclerosis, diffuse meningitis, porencephaly, or atrophy of the brain. During life the characteristic feature of these conditions consists chiefly of disturbances of motion, with spasticity of two or four extremities and arrest of intellectual development.

We will consider here two well-known forms of this disorder, viz.: infantile spastic hemiplegia and Little's disease (diplegia, paraplegia).

#### **A. Infantile Spastic Hemiplegia.—**

A spastic paralysis is noticed on one side of the body, either at birth or at the time when the child makes the first attempt to walk. In some cases the onset of the hemiplegia is acute. Fever, vomiting, restlessness, convulsions on the side which is to become paralyzed appear then first. The convulsions are epileptiform in character; they repeat themselves, and in one of these seizures the paralysis sets in. The latter is at first flaccid, but gradually spasticity develops, and then the knee-jerk becomes exaggerated; Babinski's sign, Gordon's reflex, and also ankle-clonus are easily elicited. The hemiplegia, thus established, is permanent, and presents this peculiarity distinguishing it from hemiplegia of adults: that the contractures with subsequent de-

formities are very pronounced; the hand and fingers are in a state of marked flexion, and the foot in varus equinus. Besides, the entire affected side, limbs, and their coverings, viz.: musculature, connective tissue, fat, skin, show arrested development. Even the face and thorax are diminished in size. The reduction in size is particularly noticeable in the upper extremity. The bones are atrophied not only in their thickness, but also in their length. Sensory and vasomotor disturbances are present on the affected side. The general sensations are diminished, and the skin is cold.

Infantile spastic hemiplegia is not infrequently accompanied by other special manifestations. They are: athetosis, choreic movements, epilepsy, and defects in the sphere of the special senses.

Athetosis and choreiform movements, if present, are confined to the side affected. Naturally in such cases the contractures of the limbs are not very marked. The distinction between the athetoid and choreic movements presents no difficulty, if one bears in mind that the former are confined to the fingers and wrist, and consist of slow and continuous movements increasing upon voluntary efforts, while the latter affect large segments of the limb, and consist of inco-ordinate and brusque movements.

As to epilepsy it may be confined to the paralyzed side or generalized. It appears either in early infancy or around puberty. It is a frequent complication of infantile cerebral paralysis.

Disturbances of the special senses may be deafness or eye symptoms, such as congenital strabismus and nystagmus.

Among the rarer complications may

be mentioned: defects of speech, which are due to a delayed development of the speech faculty; aphasia is extremely rare. The intellectual faculties are usually preserved, but in cases in which the frontal lobe is the seat of the chronic infantile encephalopathy, also in cases with lesions in both hemispheres, there will be an arrested mental development.

**B. Spastic Diplegia. Little's Disease.**—Diplegia, or spastic double hemiplegia, occurs when both motor areas are involved. Under pathology will be mentioned various morbid conditions which are apt to create diplegia. Should the lesion be confined only to the paracentral lobules, a spastic paraplegia of both lower extremities will be observed. All these conditions may be congenital or acquired at birth.

The congenital form was particularly well described by Little, in 1862. He pointed out that the most important etiological factor of the affection is premature labor. In these cases there is a deficient development of the pyramidal tracts. As it is well known, the latter acquire a myelin sheath only during the first few months after normal birth. Consequently, in prematurely born children the fibers of the pyramidal tracts are imperfectly developed, and stimulation transmitted to such fibers from the brain will be abnormally expressed. An increase of the muscular tonus and a rigidity of the limbs are the result.

At present authors are divided as to the definition of Little's disease. Some describe under this name both the congenital and acquired forms; others make a sharp distinction, and consider only the congenital form.

Little's disease may present itself in a paraplegic and diplegic form. The first is the more frequent.

**Infantile Cerebral Diataxia.**—J. Ramsay Hunt (Amer. Jour. Med. Sci., Apr., 1918) calls attention to a pure ataxic type of the cerebral palsies of childhood to which he gave the above name and based on 3 observed cases. Its symptomatology is characterized by a general disturbance of co-ordination without evidences of paralysis, spasticity, epilepsy, or serious mental defect. The sensibility, both special and general, is apparently unaffected. It is believed to be dependent upon a bilateral vascular lesion in the parietal region due to injury at birth. The disturbance of co-ordination affects speech, gait, station, and the use of the extremities, and is purely ataxic.

It is distinguished from cerebellar ataxia by the character of the motor disorder, its persistence in the recumbent posture, and the absence of nystagmus. It may be regarded as the sensory equivalent of the spastic type of Little, and is not infrequently encountered in combination with this affection, constituting a diataxic diplegia. As in Little's disease, there is a tendency toward improvement, although the development of motility is always seriously retarded. In its more severe forms this disorder of co-ordination may be associated with a tendency to atactiform movements which resemble superficially the phenomena of genuine chorea and athetosis.

**Paraplegia.**—The lower extremities are in a state of rigidity. Because of the latter the gait and station are characteristic. When standing, the trunk is bent forward, the thighs are in close contact with each other, while the legs are separated. In walking the feet scrape the floor and the legs have a tendency to cross each other. When the patient is seated, the feet do not touch the floor; the legs are extended. The feet are deformed and in a state of equinovarus.

**Diplegia.**—Here not only the lower, but also the upper, extremities are affected. The arms are adducted; the forearms are flexed and pronated. The

face not infrequently participates in the generalized muscular rigidity, so that when the patient attempts to speak, laugh, or masticate the facial muscles are seen to be contorted. Sometimes the muscles of deglutition or respiration are involved. The tendon-reflexes in the paraplegic and diplegic forms are increased; Babinski's sign and ankle-clonus, also, sometimes Oppenheim's and Gordon's reflexes, are present. The sensations and the condition of the sphincters are normal.

The writer observed a case in a boy 5½ years old, with abnormal laxity of the ankle joints permitting extreme dorsal flexion. There is no real muscular atony. The knee jerks are at times greatly exaggerated. At times the plantar reflexes are of the extensor type. There is an "overflow" of the abdominal reflex. The response is not limited to contraction in the muscles of the abdominal wall, but it involves considerable movement of the thighs and trunk. The condition probably dates from birth. The birth was a difficult breech presentation and some widespread damage to the cerebrum and possibly the cerebellum took place. F. Parkes Weber (Brit. Jour. Children's Dis., Mar., 1917).

The mentality in Little's disease presents some delay in development, but with proper training great improvement may be obtained.

**Cerebellar Ataxia of Children.**—L. P. Clark (Amer. Jour. Dis. of Children, June, 1913) defines this disorder as an extreme defect or disease of the cerebro-cerebellar function with relationship to bodily movements, of an unknown pathogenesis (probably based largely, if not solely, on a developmental defect) which is for the most part intrauterine in origin and which we find expressed in clinical manifestations of atonia, astasia, hypotonia, mutism and idiocy. He regards it as a distinct type of palsy of infancy. The disorder not only affects isolated movements, but par-

ticularly the association of movements or the motor synergies so-called.

In 10 cases of cerebellar ataxia in children, representing 3 types of the disease which should be identified from tumors, hemorrhage, thrombosis and softening, the writer obtained the following results: In a case due to defective or arrested development in a boy of 3½, gradual improvement was evident under **thyroid treatment, bromides, iodides, calcium chloride, valerian, mercurial inunctions, hydrotherapy and massage.** Occasional flaccid paralysis of the arm or leg was the first sign of trouble, soon after birth; the paralysis lasted for a few minutes or days and then subsided for a time, and finally came to alternate with epileptiform convulsions. Even at the best the gait was like that of a drunken man with a constant tendency to fall, but improvement was realized under the measures mentioned above while the child was for several months in the clinic, and it has continued to progress during the 2 years to date. He can now walk alone though hesitatingly. Improvement was also obtained under treatment in the 7 infectious cases; the ataxia followed typhoid, measles or pneumonia, or the parents were alcoholic. No benefit was apparent in the 2 degeneracy cases. L. Concetti (*Rivista Ospedaliera*, June 15, 1914).

**DIAGNOSIS.**—In infantile cerebral hemiplegia the rigidity of the paralyzed extremities, the contractures, athetosis or choreic movements and epileptiform convulsions, the period of life at which these symptoms make their appearance are all sufficient facts for diagnostic purposes. At the onset, however, when fever, vomiting, and convulsions are present, the disease may simulate tubercular meningitis. Here the difficulty may be great, especially when we take into consideration the fact that meningitis is sometimes followed by hemiplegia. In such cases the diagnosis

cannot be made at the beginning; the course of the affection alone will enable one to make a correct diagnosis. The disease cannot be confounded with infantile spinal paralysis, as in the latter the reflexes are abolished and the limbs are in a state of flaccidity. In birth palsy the paralysis is limited to one upper extremity, and the latter is in a state of flaccidity. The diagnosis of Little's disease presents no difficulty, especially of its diplegic form; the clinical picture cannot be confounded with other affections. The paraplegic variety may be taken for paraplegia caused by myelitis, but the latter will be recognized from the association of sphincter and sensory disturbances; also from the history of the case.

In the typical cases of infantile paralysis the legs are, of course, flaccid. In most instances they are flaccid even when there is pain. They have pain, moreover, without motion. In a certain number of cases of infantile paralysis with pain, in which there is still muscular power left because only a part of the muscles are paralyzed, there is rigidity. It is present in those cases not only during, but before, the examination, and may be marked. Personal case in which the writer could not tell whether the child had infantile paralysis or hip disease until he gave a little ether. When enough had been given to dull sensation, the leg in which the trouble was located was flaccid, while the muscular tone remained in the other. Morse (*Pediatrics*, June, 1911).

A most important sign separating these cases from others of a different nature consists of the change visible in the fundus of the eye even of infants, which may be attributed to abnormal increase in the pressure of the cerebrospinal fluid. When an intracranial hemorrhage occurs at birth, we may expect to find the appearance of recent general edema or

of a papilledema. This picture differs markedly from that seen in advanced spastics. At operation in the 80 cases observed, the dura was always found to be tense, whitish, opaque, and thicker than normal, the cortex edematous and under increased pressure. Every child whose delivery was difficult or instrumental should have its eye grounds examined by competent observers directly following its birth, whether convulsions occur or not. Kearney (*N. Y. Med. Jour.*, Feb. 3, 1917).

**PROGNOSIS.**—It is unfavorable as to recovery in all forms of infantile cerebral paralysis, but it is more serious in hemiplegia than in Little's disease. In the latter there is a natural tendency toward improvement, but recovery can never be expected. In the hemiplegic form the arrested development of the affected limbs renders the infirmity permanent. Epilepsy is a very grave complication, as it not only prevents any possible amelioration of symptoms, but retards the development of the mental faculties. According to Bourneville, the attacks of epilepsy become rarer as the child grows and often disappear at the age of 30.

**ETIOLOGY.**—Injuries to the uterus or to the head of the fetus during difficult labor with or without instrumental manipulations may produce meningeal hemorrhages and secondarily changes in the cortex. The latter are caused either directly by traumatism or by asphyxia of the newborn. Little pointed out premature birth as one of the most frequent causes of the condition. In extra-uterine life infectious diseases play a very large part in encephalitis (Strümpell). The toxins produce simultaneously grave disorders of circulation (hyperemia, hemorrhages, thrombosis, edema); also a pathological reaction on the

nervous tissue. Alcoholism and syphilis are very important predisposing factors, and, according to Bourneville's statistics, the former is a graver etiological agent than the latter. Chronic parental intoxications with lead, phosphorus, mercury are also considered as causes of the infantile encephalopathies.

During pregnancy various infections, traumata, albuminuria, alcoholic intoxication, uncontrollable vomiting, violent emotions, may all be causes of encephalopathies. At the time of conception acute alcoholism is a serious factor in cerebral disturbances of the fetus.

Four cases of cerebral paralysis in its initial stage in infants with necropsy findings. They belonged to the class of vascular lesions with hemorrhage in the brain or meninges or subdural space resulting from trauma affecting the skull or other mechanical injury before, during, or after birth, and checking the growth of parts of the brain. Cerebral paralysis resulting from actual malformation in the germinal tissue is comparatively rare, while encephalitic processes due to various infections or intestinal affections are more common. Lindemann and Marenholtz (*Jahrbuch f. Kinderheilkunde*, June, 1911).

**PATHOLOGY.**—The chronic inflammation of the meninges and sub-jacent brain-tissue (meningoencephalitis) which is characteristic of infantile cerebral paralysis may be the result of trauma, hemorrhage, or softening. Hemorrhagic or softened foci do not differ to any great extent from a similar condition in adults, with this exception, however: that the brain-tissue in the immediate vicinity of the old foci is retracted and shows depressions. The dura is thickened and adherent to the cranium, and the thickened pia is

adherent to the convolutions, so that the brain-tissue will tear if attempt is made to detach the pia from it. The encephalitis is more marked in the superficial layers of the brain than in the deep layers. The cells are found deformed, atrophied; the nerve-fibers are markedly altered, and a great many of them disappear, but instead neuroglia is proliferated.

Old meningoencephalitic foci may lead to a condition called "porencephaly." It is characterized by the presence of cavities (porus) which open on the surface of the brain. Sometimes the cavity is deep and communicates with the lateral ventricle. The latter variety is the true porencephaly, while the former is the pseudoporencephaly. True porencephaly is a congenital condition and caused by an arrest of development. Pseudoporencephaly is the result of a morbid condition leading to a destruction of brain-tissue, as, for example, in a localized circulatory disturbance. A true porencephalus presents a sort of infundibulum. Pseudoporencephalus presents a depression, whose walls are the convolutions covered by the pia mater. Porencephaly has been observed in areas having a well-defined arterial supply. A vascular influence is, therefore, the main factor in porencephaly: in the pseudo-form a hemorrhage or softening causes the destruction of tissue and a cavity; in the true form a certain artery is congenitally absent, and the brain-tissue in this area has never developed. Porencephaly is usually bilateral and found mostly in the motor area, third frontal and first temporal convolutions.

Infantile encephalopathy may present itself as an "internal hydrocephalus." This condition is a meningitis of the lateral ventricles. The ependyma is in

a state of inflammation (ependymitis), its epithelium is proliferated, the choroid plexuses are either hypertrophied or atrophied, and the blood-vessels of the latter are altered. The ventricles are overfilled with fluid, the brain-tissue which is in immediate contact with the walls of the ventricles is destroyed, and the convolutions, being under continuous pressure, become flattened and atrophied.

Atrophic sclerosis of the brain-tissue is another condition specially observed in infancy. It is the result of a congenital encephalitis. It consists of an induration of cerebral tissue. The convolutions are thin, retracted. Microscopically, the neuroglia is seen to be markedly proliferated, and the walls of the capillaries are thickened; the cells of the gray matter are either altered or totally absent. Atrophic sclerosis may affect a hemisphere, or only certain lobes, or one lobe.

Besides atrophic sclerosis the infantile brain may be affected by a "hypertrophic sclerosis." The meninges and cortex present hard nodules of various sizes. Similar nodules are also found in the white substance. Histologically, they consist of neuroglia tissue in abundance, but the cerebral tissue cells and fibers are in a state of atrophy. The various pathological conditions described above as being characteristic of infancy present another peculiarity. We know that subsequently to lesion in the brain of an adult (see Apoplexy) a secondary descending degeneration develops in the pyramidal tracts. In the fetus or in early infancy the pyramidal tract is not yet completely developed, as the myelin covering the axis-cylinders begins to appear only during the first months after birth. It stands to reason that a lesion in the brain at

those periods of life leads to an arrest of development and atrophy of the portions of the nervous tissue beneath the initial lesion. Atrophy and diminution in size of nervous tissue (brain and cord) are, therefore, characteristic of the lesions in chronic meningoencephalitis of infancy. If the lesion is in one hemisphere, the result will be hemiplegia; if the lesion is bilateral, the result will be diplegia.

**TREATMENT.**—Our means for treatment of infantile cerebral paralyses are very limited. The pathological conditions creating the palsies are beyond our means for correction.

Under Etiology (see p. 117) among various causes of spastic paralysis, dystocia was considered as a possible factor. In such cases prompt obstetrical intervention is an important measure. Pinard advises **symphysiotomy** as an excellent prophylactic method of treatment. When the labor is normal and the child presents spastic paralysis at birth, the condition is congenital and cannot be remedied. When the hemiplegia, preceded by the group of acute symptoms (see Symptomatology), appears some time after birth, the treatment will not be different from that of an apoplectic attack in an adult. Internal drugs are of no value except for epileptiform convulsions, in which case **bromides** are indicated.

It is the deformities and infirmities that we are requested to remedy. Mechanical means and surgical intervention are the only possible treatment. Statistical studies show that operations performed on the cranium and brain are not only useless, but even dangerous. On the other hand, surgery directed toward the deformities and contractures is apt to give favorable

results. **Tenotomy** and **myotomy** followed by application of **plaster casts** to the limbs put in corrected positions have given favorable results in certain cases. Various **orthopedic appliances**, **passive manipulations** of the limbs, **mobilization of the joints**, and properly regulated **gymnastics** are highly commendable for counteracting the rigidity of the muscles and of their tendons. **Massage** is a great adjuvant in this treatment; it should never be overlooked, as very good results are sometimes obtained. In conjunction with massage it is a good plan to administer frequently **warm baths**, which facilitate the reduction of muscular spasticity.

The treatment of the muscle is the all-essential in this disease. Instead of waiting for a chance recovery in the anterior cornua, and treating in a perfunctory way the muscles with massage and electricity, every affected muscle will work, provided that a commencement be made from zero. An affected limb will retain its heat, and show little waste, provided that it be rested and worked within physiological limitations, even without massage and electricity. Much patience and trouble are required, but good results are obtained in many cases. McKenzie (Austral. Med. Jour., July, 1910).

**Artificial rubber muscles** may be used to take the place of paralyzed or weak muscles. For their construction an ordinary rubber dam is used. They are chiefly applicable to the ankle, the knee, the wrist, and shoulder-joints.

By their systematic employment the lost power may be supplied temporarily until the paralyzed muscles have recovered, and contractures of opposing groups may be prevented. The rubber over the affected muscles causes a local stimulation, which is noted by active hyperemia and perspiration of the skin beneath the



artificial muscle. Its use does not immobilize the joint, nor does it interfere with other prescribed treatment, namely, passive motion, massage, or electrical contractions. Meisenbach (Med. Record, March 11, 1911).

Recently a new operation has been devised by **Foerster**, which has for object to decrease the muscular rigidity. It is based on the assumption that the increased tonus of the muscles of the limbs is dependent upon an irritation of the sensory roots of the spinal cord. Consequently a resection of the corresponding sensory roots will decrease the muscular rigidity. **Cranial decompression** in selected cases has recently gained favor.

In reporting a case of cerebral spastic paralysis due to hemorrhage, the writer gives the results obtained in his first 65 cases of **cranial decompression** for selected cases. The operated cases had been carefully selected, only those with signs of persistent intracranial pressure, less than 25 per cent. of the cases examined, being chosen. Ophthalmoscopic examination revealed dilated retinal veins and blurring of the optic disks. In the more recent cases, the presence of increased pressure was confirmed by the measurement of the cerebrospinal fluid at lumbar puncture by the use of the spinal mercurial manometer. There had been in all cases a history of prolonged and difficult labor at birth, most of them being instrumental deliveries. A negative Wassermann of both blood and spinal fluid was obtained in every case except one. No selection was made as to age, spasticity, or mental deficiency. Microcephalic children, cases of agenesis, and those due to meningo-encephalitis were naturally excluded as non-operable, there being no increased intracranial pressure.

The pathologic condition, as found at operation and post-mortem was

noted. A definite fibrous cystic formation was invariably present. This lesion was supracortical in all but 4 cases, the others being subcortical or cortical. The cysts were punctured and their outer walls removed; fibrous formation was removed except in cases in which its removal would have caused damage to the underlying tissue; in these cases it was left alone.

After-treatment consisted in the correction of deformities by **tendon lengthenings, stretching of muscles, tendon transplants, etc., massage, and careful muscle education** with special attention toward establishing an improved co-ordination.

Of the 65 patients, 9 died after operation, and 8 have died in the past 2 years, making a total of 17 deaths. The authors have been unable to obtain any record of 4 patients; 19 show practically no change; 25 show improvement more or less marked. The youngest patient was  $2\frac{1}{2}$  years of age, and the oldest 17 years.

When epilepsy is a complicating factor, the prognosis is invariably bad. The immediate results were gratifying in that the convulsive seizures were less frequent, but this improvement lasted only for a few months. The younger the child, generally speaking, the more marked has been the improvement; the older the child, the less marked. In the adult cases there had been practically none. *Supracortical lesions were the only favorable cases*; in this type damage to the nerve cells is due to pressure alone from the overlying lesion. In the cortical or subcortical lesions, there is naturally, a definite destruction of brain tissue, and only in those cells along the edges of the cyst that are suffering from pressure can any improvement be expected.

The writers urge for better preventive means in avoiding this condition. First, *more care on the part of the obstetrician* is needed; careful pelvic measurements should be made as early as possible; prolonged labor should be avoided whenever possible;

practitioners should realize that **cæsarean section** is less dangerous to mother and child than is the use of the high forceps; during the first few weeks of life every child should be as carefully inspected for symptoms and signs of intracranial hemorrhage as for deformities. When these symptoms and signs are present, cranial decompression should be performed as early as possible in those selected cases in which the fluid or clotted blood can be removed before any or little permanent damage to the brain tissue has occurred. Sharpe and Farrell (*Jour. Amer. Med. Assoc.*, lxi, 1056, 1917).

Quite a number of observations have been recorded showing satisfactory results from such a procedure in hemiplegia and Little's disease. However, the operation is serious and in several instances terminated fatally even in the hands of very competent surgeons. In the successful cases considerable diminution of spasticity was obtained, so that the patients could use their arms and legs to a certain extent. If **massage and systematic exercises** are practised after the operation, considerable benefit can be derived.

ALFRED GORDON,  
Philadelphia.

**CEREBRAL SURGERY.** See HEAD AND BRAIN, MENINGES AND BRAIN.

**CEREBROSPINAL FLUID, EXAMINATION OF.**—With the majority of diseases of the cerebrospinal system, accompanied by demonstrable changes in the cerebrospinal fluid, the diagnostic value of spinal puncture and an examination of the fluid is best appreciated, according to J. A. Kolmer (*Med. Clin. N. Amer.*, i, 355, 1917), with a complete analysis of the fluid by a physician who understands the underlying principles governing the pathologic changes which may occur. Aside from finding the

specific micro-organisms of a disease in the cerebrospinal fluid, there is no other single specific change, except first, possibly, the Wassermann reaction, which, when positive, indicates that the patient is infected with syphilis and that the nervous tissues may be involved; and secondly, the **colloidal gold reaction**, which, when yielding a typical paretic curve, indicates paresis. Even in these latter conditions other data, such as a protein determination and total cell count, are valuable in aiding the diagnosis, as exemplified in the four **reactions of Nonne**, namely, a total cell count, protein determination, and Wassermann reaction with cerebrospinal fluid and blood-serum.

In acute meningitis, the cloudy or purulent fluid in which the micro-organisms are found by smear or culture, is sufficient for diagnosis, although cell counts and protein determinations furnish data indicating the severity of the infection and serve as guides, indicating regression or progression of the disease under treatment. In practically all other conditions more complete studies, according to the following outline, are necessary before the full value of a cerebrospinal fluid examination is to be gained: 1. Pressure as taken with the Landon manometer and in a uniform manner, preferably with the patient lying on the left side. 2. Physical appearance of the fluid. 3. Total cell counts made with fresh warm fluid and preferably with the Fuchs-Rosenthal chamber. 4. Differential cell counts made with direct smears of the sediment secured by thorough centrifugalization or by the Alzheimer method. 5. Protein determination, employing the Noguchi or Kaplan tests. 6. Sugar determinations, employing the simple and rather crude Fehling's reagent or the more accurate micro-method of Bang. 7. The Wassermann reaction, employing graded amounts of fluid up to and including a dose of at least 1.5 c.c. 8. The Lange colloidal gold test, employing an acceptable reagent. 9. Bacteriologic examinations if the presence of bacteria are suspected; by direct examination of stained smears of sediment or cultures of the sediment on appropriate culture-media. Animal inoculation tests may be used for detection of tubercle bacilli and spirochetes.

**TESTS.**—It was not until quite recently according to A. L. Skoog (N. Y. Med. Jour., June 23, 1917), that the source of the cerebrospinal fluid was ascribed to the cells of the choroid plexus gland. The normal pressure ranges from 100 to 150 millimeters in the sitting posture. The vast majority of *pathological pressures* are above normal. Brain tumors have the highest pressure, often ranging from 600 to 700 millimeters. In tubercular meningitis it is not quite so high.

According to A. M. Moody (Chicago Neurol. Soc.; Jour. Amer. Med. Assoc., Jan. 17, 1914), **Lange's colloidal gold test** is most valuable for diagnostic purposes. A series of ten test-tubes is used, 6 by  $\frac{3}{4}$  inch in size. In the first, place 1.8 c.c. of a 0.4 per cent. sodium chloride solution, freshly made from a stock 10 per cent. solution in one test-tube, and 1 c.c. in each of the other nine. Then take 0.2 c.c. of yeast and add to the first two. This is mixed with a 1 c.c. pipet. One c.c. is removed and added to the second tube, making a dilution in this tube of 1:20. This procedure is carried on throughout the series. When finished, there is 1 c.c. in each tube, varying from 1:10, 1:20, 1:40, and so on up to 1:5120 in the last tube. Making the indicator requires great care. When good, it is clear red, with some yellow and a tinge of purple.

The tests should stand for 24 hours that the maximum reaction may be secured; nevertheless, within from 15 to 30 minutes one can tell what the result will be. He divides the reaction into 3 groups: (1) the reactions which are strongest in dilutions of 1:40 and 1:80; (2) those having the maximum reaction in dilutions of 1:80, 1:160 and 1:320; (3) those reactions which are strongest in dilutions of 1:640 up to 1:5120. Diseases of the brain and cord falling into the first class are those due to syphilis, namely, syphilitic meningitis, gumma of the brain, tabes dorsalis, general paresis and congenital syphilis. Tuberculous meningitis usually gives the strongest reaction. Brain tumor, toxic meningitis and edema from sunstroke may give a slight reaction of equal intensity. The Lange reaction runs parallel with the Nonne. It bears a close relationship to the Wassermann reaction.

The removal of blood from normal dogs followed by the intravenous injection of human syphilitic serum in amounts varying from 30 to 50 c.c. per kilogram of body weight was followed by the presence of small amounts of syphilis reagin (the antibody concerned in the Wassermann reaction) in the cerebrospinal fluid. The reagin was found in the cerebrospinal fluid as early as 3 hours after transfusion with syphilitic serum. While it is possible that in human syphilis the presence of traces of reagin in the cerebrospinal fluid may be due to the passive transfer of this substance from the blood, as shown by Wile and Stokes, the presence of the reagin with or without other changes in the fluid, as an increase of protein and cells, usually indicates the presence and activity of *T. pallida* in the tissues of the central nervous organs. Kolmer and Sekiguchi (Jour. of Immun., Mar., 1918).

As an index of pathologic change in the cerebrospinal fluid of children, the writer found that the colloidal gold reaction is more delicate than any other test. Johnston (Amer. Jour. Dis. of Children, Aug., 1916).

The writer pointed out that among the clinical cases of uremia, all those showing a *high urea content* in the spinal fluid were fatal. Most of those with low urea content survived, and in several the diagnosis was found to have been erroneous. R. G. Canti (Lancet, Feb. 12, 1916).

The **colorimetric method** of determining the hydrogen ion concentration of the cerebrospinal fluid, according to Hurwitz and Tranter (Arch. of Internal Med., June, 1916), gives constant and reliable results.

Boveri's color test was tried by Chiara-vallotti (Pediatria, Oct., 1917), in 30 cases of various meningeal troubles and normal controls. He found it easy technically and reliable at the bedside. It is as follows: To 1 c.c. of the cerebrospinal fluid is added 1 c.c. of a 1:1000 solution of potassium permanganate. If the cerebrospinal fluid is normal, the violet tint persists unmodified for some time. With a pathologic fluid, the tint turns yellowish, and

the sooner and more intense the phenomenon, the more pathologic the cerebrospinal fluid. His own technique differs slightly from Boveri's as he uses only 1 drop (0.05 Gm.) of a decinormal solution of potassium permanganate for 1 c.c. of the fluid, shaking up the test tube. S.

**CEREBROSPINAL MENINGITIS.** See MENINGITIS, CEREBROSPINAL.

**CERIUM OXALATE**, *cerii oxalas*, is in reality a mixture of this salt with other rare earths, of which didymium and lanthanum are the principal. It occurs as a fine, white powder, devoid of taste or odor. Being insoluble in water, alcohol, ether, and other fluids, it is administered as a powder.

**DOSE.**—The U. S. P. gives the average dose as 1 grain (0.065 Gm.), but this is insufficient in most cases, 3 to 5 grains (0.2 to 0.3 Gm.) being necessary in adults to obtain beneficial results.

Personal experiments have shown that it ought to prove efficacious in alleviating all those conditions for which bismuth is now used. It may inhibit vomiting due to local irritation of the gastric mucosa, but only if given in large doses for some time, so as to coat the stomach wall pretty generally.

Cerium oxalate is not absorbed from the gastrointestinal tract. Most men prescribe cerium oxalate in too small doses, 2 to 3 grains (0.13 to 0.2 Gm.). Since it accomplishes its purpose by mechanically coating the walls of the stomach, it should be given in doses comparable to those of bismuth subnitrate. Baehr and Wesler (Arch. Int. Med., Jan. 15, 1909).

**PHYSIOLOGICAL ACTION.**—The actual mode of action of cerium oxalate has not been studied sufficiently to warrant any positive statement, but it probably corresponds with that of bismuth. Its action is purely local, none, as far as we know, being absorbed. It is apparently non-toxic, ½ ounce (15 Gm.) having been taken in six hours without apparent effect.

**THERAPEUTICS.**—Cerium oxalate has proven most effective in vomiting of preg-

nancy and of uterine irritability. In alcoholic gastritis and other forms of gastritis or gastric neuroses it is also very helpful.

The writer has been using cerium oxalate largely in cases of vomiting due directly to gastric disease, usually giving 6-grain (0.4 Gm.) doses three times a day in adult patients, combined with 10-grain (0.65 Gm.) doses of carbonate of bismuth. In almost every case the result has been most satisfactory, and in several instances, when bismuth alone has failed to cause any marked improvement, a rapid change for the better has appeared when cerium oxalate has been added to the medicine. In gastric ulcer the pain is relieved and the vomiting ceases almost immediately; the same result occurs in chronic catarrhal gastritis, especially the form which is so common among badly nourished young women, whose work deprives them of their proper quantity of fresh air. In cancer of the stomach, apart from cases in which pyloric cancer causes obstruction, although a permanent cure cannot be expected, the symptoms are relieved and the patient's life is prolonged and made far more comfortable than by any other means; the pain is lessened, hematemeses ceases, and the patients who have been unable to retain the smallest quantity of food taken by the mouth are soon able to retain several pints of milk per diem, and also small quantities of the prepared farinaceous foods. Sweetman (Dublin Jour. Med. Sci., Feb., 1906).

In seasickness it has given excellent results, but only when administered in large doses—10 to 15 grains (0.6 or 1 Gm.) or more every two or three hours. Its use has also been extolled in pertussis, migraine, harassing hiccup, and also in the gastric crises of tabes. S.

**CHALK.** See CALCIUM.

**CHANCRE.** See SYPHILIS.

**CHARCOAL** (*carbo*) is used in medicine in two forms: charcoal (*carbo ligni*, U. S. and B. P.), which is obtained

by exposing soft wood to a red heat with a minimum of air, so that smoldering rather than rapid burning occurs, the resulting product being black, shining, odorless, tasteless, and insoluble, and animal charcoal (*carbo animalis purificatus*), prepared by treating bone with hydrochloric acid, which removes the bone phosphates and calcium carbonate, and washing. It occurs in dull, black fragments or powder, is odorless, almost tasteless, and insoluble in water or alcohol.

**PREPARATIONS AND DOSE.**—The drug, for internal use, is finely powdered, and either form should be given in the dose of 20 grains to a dram (1.3 to 4 Gm.). For external use the powder may be used, or a poultice may be made of powdered charcoal,  $\frac{1}{2}$  ounce (15 Gm.); bread crumbs and linseed meal, 2 ounces (60 Gm.) each, and enough hot water to make the mass of the desired consistency.

**THERAPEUTIC USES.**—Charcoal is used for clarifying and decolorizing solutions and makes a splendid filter, water passed through it losing all its impurities. Being a deodorant, disinfectant, and absorbent, it is an efficient application to **foul sores, ulcers, broken-down cancerous growths, gangrene, etc.**, and for this purpose either the powder or the above poultice may be employed. Finally, powdered charcoal makes an excellent dentifrice. Carbon tetrachloride ( $\text{CCl}_4$ ) is anesthetic and has been used in **asthma**, by inhalation.

Charcoal absorbs bacterial toxins both in the test tube and in the living body. **Dysentery** toxin, for instance, has its toxic properties nullified by the charcoal as effectually as by an antitoxin. Kraus and Barbara (Wien. klin. Woch., May 20, 1915).

Internally, it is used to absorb gases and offending products of digestion. Thus, it is a useful remedy in **flatulence, pyrosis, sour stomach, Asiatic cholera, nausea of pregnancy, and in acid diarrheas.**

For **hyperacidity and pyrosis**:—

$\mathfrak{R}$  *Sodii bicarbonatis* . . gr. x (0.65 Gm.).

*Magnesi carbonatis*. gr. xv (1 Gm.).

*Carbonis ligni*. . . . . gr. x (0.65 Gm.).

**Sig.:** Mix and take in  $\frac{1}{2}$  glass of water (hot) immediately after retiring. W.

## CHEST, INJURIES AND SURGICAL DISEASES OF THE.—

Under this head will be considered the various surgical diseases of the lungs and pleura, heart and pericardium, thoracic duct, chest wall, and pulmonary artery and the various surgical procedures indicated for the treatment of these conditions.

### WOUNDS OF THE PLEURA AND LUNG.

Injuries of the pleura and lung are considered together, owing to their anatomical relationship. *Contusion, laceration, and often rupture* may occur without fracture of a rib or any other evidence of injury to the chest wall.

**Contusion.**—Soreness, pain, cough, and, in rupture of the lung, hemoptysis, pneumothorax, hemothorax, or emphysema may be present. It is difficult to predict, however, the results that may attend a fall, blow, or crush. While a blow over the heart or below the xiphoid cartilage may produce instant death, a heavy team has passed over the chest of a child without more than a slight superficial bruise and soreness. Shock is present, however, in practically every case, with pallor, prostration, and syncope as most evident symptoms. Pleurisy with effusion or bronchitis may develop, while a fractured sternum or fractured ribs may evoke complications involving any of the thoracic organs, including the heart.

Explosion of a large projectile 2 or more yards away may produce slight or serious lung injury in the absence of any external wound. Léon Binet (Presse méd., Mar. 23, 1916).

**Stab Wounds.**—Such a wound, with a clean knife, into the periphery of the lung, away from the large vessels, is

usually followed by prompt healing; in the root of the lung it may cause rapid death from hemorrhage, while an infected wound anywhere is liable to result in pneumonitis, pleuritis, or empyema.

Lawrow in commenting on 257 cases of stab wounds of the thorax observed in the years 1905 to 1909, inclusive, states that the great majority of penetrating wounds of the chest, the diaphragm, and abdominal organs, the heart and pericardium and the blood-vessels of the thorax are involved. In 155 cases operated upon, 78.5 per cent. exhibited lesions of the inner organs: diaphragm, 35.4 per cent.; heart and pericardium, 9 per cent.; lungs, 27.7 per cent., and the vessels of the thoracic wall, 6.4 per cent. Lesions of the mediastinum and isolated pleural lesions were observed in 21.5 per cent.

**Gunshot Wounds.**—While primary hemorrhage is not so likely, yet secondary hemorrhage and infection are more likely to follow gunshot wounds of the lungs, as fragments of clothing are often carried in and the lung-tissue torn and bruised and placed in conditions favorable to the development of infection. Recent wars as well as experience in civil practice have shown us that a perforating bullet wound of the chest and lung is often followed by speedy recovery without complications. At other times a bullet will act like an explosive body—either by the momentum communicated to fragments of bone it may have made or from its own size and momentum, and the lung will be greatly injured.

Two wounds on opposite sides of the chest do not necessarily mean perforation of the lung, as balls often deviate from their course on striking a rib or fascia and follow the rib part way around the chest, remaining lodged in the tissues or escaping

through the skin at some point distant from that of entrance. Sometimes the ball simply penetrates the pleura and drops into the pleural cavity, where it may become encysted or give rise to trouble requiring its removal.

Pyrexia is common, but does not always mean infection. The latter should be suspected when the evening temperature is high, daily excursions wide, and general symptoms severe. Removal of some of the fluid may accelerate absorption of the rest, but it is usually wise to take away as much as possible. After **aspiration of blood** there is no reaccumulation. W. Hale White (*Lancet*, Dec. 4, 1915).

There is a sound heard on auscultation in cases of penetrating wounds of the chest near the cardiac region which is unlike anything met with in civil practice. It is of the nature of a click, and varies from a faint sound heard by careful auscultation, to a noise which may be compared to that heard in the ear piece of a telephone when the lever is moved up and down. It may be heard sometimes when standing at the foot of the patient's bed. S. M. Smith (*Brit. Med. Jour.*, Jan. 19, 1918).

Hemothysis, pneumothorax, and emphysema following either a stab or gunshot wound of the chest would be good evidence that the lung had been wounded, though it must be borne in mind that air entering from the outside may cause pneumothorax or emphysema. A large wound opening the pleural cavity would probably give rise to traumatopnea, or, possibly, to hernia of a part of the lung. Hernia or prolapse may come later as a result of coughing, straining, or of cicatricial formation. Some authorities distinguish between hernia and prolapse of the lung. Prolapse occurring through an open wound through the skin and

other tissues should be treated by reduction and closure of the wound when possible, or removal of the prolapse by ligation or excision and suture, and then closure of the wound.

In a study of 53 followed up cases of penetrating chest wounds in soldiers, the writer found the symptoms strikingly constant in 25 uncomplicated cases, varying only in intensity and duration. Over the inferior third of the wounded lung, posteriorly, an area of dullness with resistance to the finger, loss of vocal resonance, and indistinctness or loss of breath sounds, were noted. Above this area was another of diminished resonance, with preserved or increased vocal resonance, but in particular, with distinct bronchial breathing at times slightly veiled. Fluoroscopic examination showed a shadow very dark below over the lower two-thirds of the lung, and exploratory puncture, an intrapleural accumulation of blood. Hemoptysis, the most characteristic functional sign, was present in 56.7 per cent. of the cases. Primary hemoptysis is carefully distinguished by Piéry from secondary hemoptysis, which sets in only on the second or third day and in which not fresh blood, but blood mixed with mucus and serum, is got rid of. Fever beginning 12 to 48 hours after the injury, persisting about two weeks, and then declining by lysis, was a striking feature, signifying a pneumonic process, more or less marked. Piéry (*Presse méd.*, June 3, 1915).

In 107 cases of chest wounds produced by rifle or machine gun bullets (45) or by shell as shrapnel, high explosive or hand grenade (42), the writer found the symptoms were cough, pain, hemoptysis of varying degree, and dyspnea. There was usually fever. The physical signs suggested consolidation rather than fluid, owing to the great compression of the lung. Cardiac displacement was often striking. In 8 cases there were unequivocal, and in 5 others suggestive signs of pneumothorax. In 4

cases pneumonia existed on the side opposite to the hemothorax. Secondary hemorrhage into the pleural cavity occurred in 1 case only. Simple fibrinous pericarditis occurred in 3 cases, and in 1 a pneumopericardium. C. P. Howard (*Amer. Jour. Med. Sci.*, Nov., 1916).

Out of 110 cases of perforating wounds of the chest under observation in a military hospital for a period averaging 10 days, only 12 deaths took place. Six of these 12, moreover, had other wounds which compromised the issue. But little difference in mortality was noted between the cases in which a point of exit of the bullet or other missile was manifest and those in which the foreign body remained. Complications included protracted hemoptysis in 8 cases, hemopneumothorax in 25, empyema in 12, lung congestion and bronchopneumonia each in 5, friction rubs in 4, simple bronchitis in 3, and lung abscess with hernia in 1. Remond and Glénard (*Paris méd.*, Nov. 6, 1915).

*Hernia of the lung or pneumocoele* is the name applied when a part of the lung protrudes through an opening in the thoracic wall beneath the unbroken skin. It may occur from the yielding of a cicatrix or suddenly from the rupture of the intercostal muscles and pleura, and protrudes most frequently about the fifth intercostal space or root of the neck, appearing as a round swelling, giving a crepitant sensation to the fingers, increasing in size with respiratory efforts, diminishing or disappearing on holding the breath, and giving a vesicular murmur on auscultation. A pad or truss may be used, but it would seem that in suitable cases an operation for radical cure should be done.

The writer emphasizes the value of stereoscopic radiograms in locating foreign bodies, also the fallacy of at-

tempting to determine from a single radiogram the exact location of foreign bodies, and also that of attempting to form a correct view of the position of fragments after a fracture. E. G. Beck (*Interstate Med. Jour.*, xxiii, 259, 1916).

A series of 211 cases of gunshot wounds of the chest observed in France and England showed that the most important part of the X-ray examination of the chest was to inspect the 2 domes or cupolæ of the diaphragm. The right dome cannot be distinguished from the shadow of the liver except when a subphrenic collection of gas is present. The left dome is normally defined by the gastric gas bubble. There is usually a deficient movement of the diaphragm in a perforating wound of the thorax and frequently there is complete immobility. The latter condition is also an accompaniment of lung collapse, being found on the same side as the collapse. If an opaque lung area is present in the supradiaphragmatic area it may prevent observation of the movements of the diaphragm. If the opacity be due to fluid, the diaphragm may be visible in the lying position. On the left side the presence of a stomach gas bubble will enable one to note the position and movement of the diaphragm where the left lung area is opaque. P. T. Crymble (*Brit. Jour. Surg.*, v, 363, 1918).

In making the diagnosis of wound of the lung the probe should be used with great care if used at all. If it is pretty clear that the lung is wounded the probe is unnecessary. In doubtful cases it may be used to ascertain if the wound has penetrated the chest wall into the pleural cavity. It is important to determine the source of blood escaping from a wound in the chest, especially whether it comes from an intercostal vessel or from a wound in the lung itself. This may often be done by inspecting the edges

of the wound, enlarging it if necessary in order to do so.

Hemothorax is the most common result of a chest wound, pneumothorax and hemothorax being rare. The hemothorax may be sterile or infected. Infection may occur as late as the second or third week, onset characterized by fever, dyspnea, pain, etc. In a series of 450 cases observed by Bradford and Elliot, infection was present in 117, the pneumococcus and bacillus of influenza being present in 20 per cent., and streptococci, staphylococci, and anaerobic gas-forming bacilli in the remaining 80 per cent. Anaerobic bacilli were present in 50 per cent. of the infected cases. J. R. Bradford (*Brit. Med. Jour.*, ii, 141, 1917).

In 165 cases of penetrating chest injuries there were 30 deaths, 18.68 per cent. Aside from multiple lesions other than the thoracic injury there were 154 isolated thoracic wounds with 20 deaths, 12.91 per cent. There were 27 cases of open thorax with 6 deaths, 25.8 per cent., and 127 cases of closed thorax with 14 deaths, 11.11 per cent. The mortality was higher in the first 48 hours. It was especially high in wounds with largely open thorax; 5 out of 10 died. When the thorax was less widely open the pleura was frequently secondarily infected, particularly when the wound trajectory was long.

An important complication was the rapid early development of septic pleuropulmonary accidents; 7 deaths were so caused in from two to ten days. Another important complication was mediastinal emphysema. Gatellier and Barbary (*Bull. et mém. Soc. de chir. de Paris*, xliii, 509, 1917).

Dyspnea is frequent as a sequel of war wounds of the chest. It is sometimes continuous, sometimes intermittent or brought on by exertion, and it may be of mechanical, nervous or reflex origin from some chronic inflammation or sclerosis of lungs or pleura, or some lesion in the diaphragm or mediastinum. It was observed in about 40 per cent. of the



writers' cases of war wounds of the chest from 6 months to a year or more after the injury. The dyspnea assumed the type of asthma in from 2 to 5 per cent. Loeper and Codet (*Progrès méd.*, Sept. 1. 1917).

**Treatment.**—Contusions, lacerations, or rupture of the lung without external wound are treated by confinement to **bed** and **light diet** until the fever and pain disappear. Any accumulation of air and blood in the pleural cavity in such cases can usually be left alone in full confidence that it will be absorbed within a reasonable time. A serious injury capable to any degree of involving complications imposes the duty of keeping the patient in bed. All symptoms should be carefully noted at short intervals, particularly those elicited by physical examination of the thoracic organs, the lungs, heart, etc., several days after the injury.

The immediate treatment should be addressed to the shock, including the use of **saline solution** and **adrenalin** intravenously. **Stimulation** is also necessary. **Morphine** to subdue pain is of great value, since it helps to keep the patient quiet, an important feature of the cases. Any complication must, of course, be met.

The two greatest dangers in *stab* and *shot* wounds of the lung are hemorrhage and infection. In such wounds unless the bleeding requires immediate operation an **antiseptic dressing** should be applied to the wound or wounds without making any attempt to disinfect them, and the patient put at rest in bed as soon as possible.

In the present war the immediate symptoms following lung injury were so severe that the operation had to be postponed in most cases. The

writer, found the patient so well the next day that the indications for operation were absent; in most cases a gradual recovery resulted. Out of 24 cases so treated only one died, all others making uninterrupted recoveries, with the exception of 3—emphysema 1, removal of bullet 2—in whom surgical intervention became necessary later on. The case that died showed interesting findings at autopsy. The wound in the lung had closed spontaneously, hemorrhage had ceased, and the blood in the pleural cavity was sterile. The bullet had lodged in the pericardium and had caused a suppurative pericarditis, to which the patient succumbed. Rühsamer (*Beitr. z. klin. Chir.*, xciii, 647, 1914).

Primary hemorrhage is the chief cause of death during the first few hours after the receipt of a wound of the chest. When severe, the patients are brought in blanched, restless, and with a rapid pulse. Restlessness is the most marked feature of the case. The treatment for these bad cases is mainly expectant, keeping the patient as **quiet** as possible and easing pain by the use of **morphine** or **heroin**. They require very careful handling, rolling them over on to their sound side to dress the wound being sometimes sufficient to cause death. The blood usually comes from the deeper blood-vessels in the lung, and Nature's method of arresting it is to cause collapse of the lung. Rees and Hughes (*Lancet*, Jan. 5, 1918).

Hemorrhage, when originating from the chest wall was formerly arrested by ligating the intercostal or mammary vessels or by padding the wound with gauze.

Extensive experience at an advanced operating center showed that severe hemorrhage never arises from the intercostal arteries, and the practice of plugging the opening is of no value in controlling the bleeding, and may be of material harm in preventing free ingress of air and the col-

lapse of the lung, which is Nature's method of promptly controlling the bleeding. The plugging is also a frequent means of transferring infection to the interior of the chest. While a large proportion of all penetrating or perforating chest wounds are probably accompanied by the introduction of infection through the missile and the clothing, in the majority of cases the pleura can care for this infection provided further infection is prevented. Rees and Hughes (Lancet, Jan. 12, 1918).

Hemorrhage from the lung itself is more difficult to deal with. If the wound is already large enough to expose the lung so that the bleeding point can be seen, the lung-tissue may be carefully sutured with catgut or a ligature may be applied. If the lung cannot be seen, the surgeon must decide between making a large opening with a chondroplastic flap or a smaller opening by resecting a part of one rib. In the former method he may find the bleeding area in the lung and secure it; otherwise, he must stop the bleeding by packing gauze in the pleural cavity. In the latter method he has no choice but to use gauze packing to compress the lung till the bleeding is controlled.

Recently various drugs have been employed as hemostatics. The striking results obtained from **amyl nitrite** in the hemorrhages of tuberculosis suggest to Steel that its sphere of usefulness can be enlarged, and that hemoptysis, either primary or secondary, resulting from penetrating wounds of the lung can be similarly successfully treated.

Dupont and Troisier (Bull. et mém. de la Soc. méd. des hôp. de Paris, Nov. 27, 1914) reports 3 cases of penetrating rifle bullet wounds of the thorax with hemoptysis, in which **emetine** was used with good results.

In 122 cases the importance of **early and prolonged immobilization** in treatment of wounds of the chest is urged by

Maillet (Annales de Méd., Mar.-Apr., 1916). **Gelatin, calcium chloride** and other measures to check hemorrhages were supplemented by **emetine**. In 1 case **artificial pneumothorax** succeeded when all else had failed. These patients are particularly sensitive to getting chilled, and they develop serious congestion on the slightest exposure. **Quinine** was given in the cases with congestion. EDITORS.

In a report on the use of artificial pneumothorax in chest wounds, the writer states that of 290 penetrating chest wounds, there were with closed chest, 206. Of these 206 cases, 88 were treated by pneumothorax, and 118 by thoracocentesis and pneumothorax, with a mortality of 7 or 3.4 per cent. Of these, 3 were due to empyema, 1 to pulmonary abscess, 3 to septicemia. Of 84 cases of open chest wounds, 19 or 22.6 per cent. terminated fatally. Of the 19 dead, 1 patient died before reaching the hospital, 7 patients had bled and were shocked so severely that nothing but, perhaps, transfusion could have helped them. Subtracting these 8 cases, there remained 76 in which the treatment could be tried. In these 76, there were 11 deaths or 14.4 per cent. Of these, 7 were due to empyema, 4 to septicemia. Empyema occurred altogether 11 times but only in the cases treated by permanent closure of the parietal wound with the rubber bag. Since this procedure has been resorted to for emergency only and the wound has been sutured airtight according to the writer's principles, only 2 deaths or 5.7 per cent. occurred in 35 cases. Bastianelli (Jour. Amer. Med. Assoc., from Surg., Gynec. and Obstet., Jan., 1919).

Another measure which has proven effective in many instances is the **admission of air** into the pleura through an artificial opening, *i.e.*, **artificial pneumothorax** (see also page 130).

That none of 100 soldiers with gunshot wounds of the lungs examined or treated from 5 to 20 days

after injury died is ascribed by the writer to his practice of **puncturing the chest cavity** and letting in air. This aids in expelling secretions, tends to prevent bleeding, and reduces the tendency to retraction and adhesions. Ehret (Münch. med. Woch., Apr. 20, 1915).

Of 190 chest injuries treated in Army Hospital No. 8, 25 died of shock before they became operable. There were 16 deaths, a mortality of 40 per cent. In 43 cases a major thoracotomy and some operation on the lung were performed. In this group there were 27 deaths, a mortality of 63 per cent. Eighty-two cases of perforating wounds; 7 patients died, a mortality of 8.5 per cent. The total mortality in cases in which the thorax was opened at the time of injury was 39.5 per cent. The time elapsed after injury averaged 16 hours. The wounds were heavily infected, 40 per cent. showing streptococci and nearly all anaerobes. Shipley (Amer. Jour. of Surg., xxv, 221, 1921).

Artificial pneumothorax has been particularly used by Italian surgeons. According to Bastianelli of Rome (N. Y. Med. Jour., Jan. 11, 1919), Major Morelli introduced **artificial pneumothorax** into the Italian army, leaving the complete chest operation for the treatment of exceptional cases. Some lung wounds are such that air is not admitted to the pleural cavity from the outside, neither can it escape, so that both hemothorax and pneumothorax are in a closed thorax, and when there are no adhesions generally the hemorrhage is either fatal, profuse, or moderate; it may not be apparent at the beginning, but ultimately appears and is prolonged. This prolonged hemorrhage is due to the fact that inside the closed thorax the negative pressure of the lung works like a suction cup on the lung wound. There are then two morbid conditions—movement of the wounded organ and suction on the wound itself. In many such cases of closed thorax wound Nature may effect a perfect or an imperfect cure. The mechanism of the cure by Nature is through the *pressure exercised on the lung wound by the blood in the pleural*

*cavity, by the air, or by both together.* With 1500 or 2000 c.c. (3 to 4 pints) of blood inside the pleural cavity the lung can still expand. The lung, collapsed and immovable, presents a favorable condition for healing.

Yet blood in the pleural cavity is dangerous not only as a medium for microorganisms, but also for the formation of fibrous tissues which obliterate the pleural sinuses and produce adhesions. Nor does its presence favor expansion of the other side of the chest. If instead the pleural cavity is filled with air, the lung is compressed, hemorrhage, infection, and adhesions are prevented more easily, and even a large missile inside the lung may sometimes remain without complication provided immobility is maintained. With blood in the pleural cavity the lung is usually only partially retracted and there are bad functional consequences. If the lung is surrounded completely by air, adhesions do not occur,

Adhesions may occur later, but the lung having already expanded the function is good. Hence it was deemed advantageous to remove the blood as completely as possible from the pleural cavity and to substitute air. Secondary hemorrhage was never seen. The current opinion that blood in the pleural cavity checks hemorrhage is not true; this occurs only if air is substituted, inducing a sufficient pressure to cause collapse of the lung. When a lung wound is demonstrated pneumothorax should invariably be performed.

The contradictions are: Adhesions preventing the introduction of air or when air escapes through a gap of the chest wall, which can not be completely closed, or through the lung wound itself. But these conditions are exceptional. Closure of the open chest should be made as promptly as possible, with introduction in the chest wound of a small rubber bag which, when inflated, seals the opening completely. These bags and the apparatus for performing the pneumothorax, were devised by Major Morelli.

In 206 cases of lung wounds with closed chest treated by pneumothorax alone or by thoracentesis and pneumothorax there were but 7 deaths. Among the cured cases only 22 showed complications. Of

the open chest there were 84 cases, with a mortality of 19—i.e., 22 per cent. Of the 76 treated by pneumothorax after removal of the blood there was a mortality of 11 cases—14½ per cent. There had been great improvement in this series since Professor Bastianelli's plan had been systematically adopted, i.e., that of suturing the chest wall airtight instead of permanently plugging the gap with the rubber bag. In 35 cases so treated there had been 2 deaths.

The approximate mortality from gunshot wounds of the chest during the European war was at all parts of the line of communication 20 per cent., according to Moynihan (Surg., Gynec. and Obstet., Dec., 1917). The causes of death were hemorrhage as a rule within 28 hours, and sepsis after the third or fourth day. The local conditions in wounds of the chest wall and lung were in all respects similar to those met with in wounds elsewhere. The lung tissue is more resistant to attack than many other tissues. The opening of the pleural cavity and the resulting exposure of a large serous sac to infection and all its consequences add, however, a danger of the most threatening character. The chief essential in the treatment of all cases of penetrating wounds of the chest is **rest**. In clean perforating wounds of the chest, rest together with the **cleansing and dressing of the wound** of entrance or exit, will lead to the recovery of the great majority of cases. In cases of "open thorax," the **earliest and most complete effort possible** must be made to secure **closure of the wound after an appropriate toilet**. In cases of hemothorax when the blood effused is small in quantity and remains sterile, no active measures are necessary, according to Moynihan, unless absorption is long delayed. **Aspiration**, repeated if necessary, may then be performed. In cases of hemothorax, when the blood effused is large in amount and remains sterile, aspiration after the seventh or eighth day, or earlier in cases of urgent dyspnea, certainly hastens convalescence, permits a more rapid expansion of the lung, and prevents the formation of firm adhesions which may permanently cripple the free movements of the lung. In cases of hemothorax,

whether the amount of blood is small or large, when infection takes place, open operation is necessary. Early operation both when the **Carrel-Dakin technique** or **Morison method** are adopted saves many weeks of convalescence and permits of a more perfect functional recovery.

Small foreign bodies, or rifle bullets, imbedded in the lung, often cause no symptoms; they become encapsulated and may safely be left. Larger foreign bodies retained in the lung may cause distressing or disabling symptoms for long periods. In such cases removal after resection or elevation of the fourth rib through an anterior incision will allow of the safe **removal of the projectile** from any part of the lung. Pieces of metal so removed are almost always infected. Pierre Duval of Paris, in 1916, advised this procedure. He effects a wide penetration of the pleura, with total pneumothorax, which does not present any particular danger when the cardiopulmonary apparatus is normal.

The writers recommend **local anesthesia** for operations on the chest having extracted a projectile from the lungs under it in 30 cases, and emphasize the ease and simplicity of the procedure. It affords better control of pneumothorax while reducing the operative shock and disturbance to the minimum. They had no accidents nor mishaps. They flood the field of operation with a weak antiseptic solution, resect ribs and gain access to the lung without dread of operative pneumothorax. Couteaud and Bellot (Bull. de l'Acad. de Méd., July 18, 1916).

The **operative method** should be preferred to the use of the **electromagnet** for the extraction of portions of projectiles retained in wounds or cavities. In the trachea, esophagus, and intrathoracic regions, however, in which operation is difficult or impossible, extraction of the foreign body must be made generally by means of the **electromagnet**. Burk (Deut. med. Woch., xlii, 134, 1916).

From a study of 50 cases to their ultimate conclusion, as to whether or not a **foreign body** in the chest

should be **immediately removed**, the writer concludes affirmatively in all cases showing a foreign body deeper than the ribs are included, irrespective of whether or not they had penetrated the lung. But 2 died. In the case of 1 an abscess formed around the foreign body. The abscess was drained and the foreign body removed. The patient died from hemorrhage on the eleventh day after operation. The other patient died 3 days after the removal of a rifle bullet from the lung, apparently from pulmonary thrombosis. R. D. Rudolf (*Lancet*, cxciii, 709, 1917).

The removal of the foreign body from the lung is only justifiable in a few selected cases, but the sewing up of the wound is advisable in all cases of leaking chest wounds, since it is by this means one can prevent the pleural cavity from becoming infected in more than half the cases. The treatment of the cases of closed pneumohemothorax differs in no way from that of an ordinary hemothorax. The authors had 72 cases of hemothorax and closed pneumohemothorax with 14 deaths, a mortality of 19.3 per cent. Of the fatal cases, 5 patients died from primary internal hemorrhage. Of the 67 patients that survived 48 hours, 8 became infected (11.9 per cent.) and 5 died from this cause, a mortality rate of 7 per cent. Bronchopneumonia caused the fatal result in 1 patient, and heart failure in 2. Rees and Hughes (*Lancet*, Jan. 5, 1918).

There are 2 processes that permit exact localization of a foreign thoracic body and its extraction. For locating, the X-ray usually suffices; but even here the radiologist may at times admit that the electro-vibrator may be of use. The vibrator is however of particular use during the extraction; it takes the place of the X-ray and it is here that it interests the surgeon. Extraction with the aid of the electro-vibrator is more practical than extraction under fluoroscopic screen control or with the use of the compass.

There are some limitations due to the kind of metal composing the projectile and its size and depth. Magnetic bodies alone can be located by this method; and if too deeply embedded, even these may not set up oscillations in the instrument. Grégoire and Bergonié (*Trans. Assoc. française de chir.*, 1918; *Surg., Gynec. and Obstet.*, Mar., 1919).

Signs of infection, such as elevated temperature with or without chill, require opening of the pleural cavity, preferably through the wound tract, the removal of septic material, foreign bodies, and the establishment of efficient drainage. The recent war has introduced many innovations in this direction likewise—a complete transformation, in fact, of older views—the most important of which is Duval's, previously referred to.

The writer calls attention to the fact that in the last 2 years the treatment of lung wounds in the French army had changed from the medical to the surgical. This surgical treatment consisted in excising the lung wound and treating it as one would a wound in any other part of the body. The chest was opened widely enough to take the lung out; it was examined on all its surfaces; hemorrhage was checked, the lung replaced, and the chest wall sutured completely. In the first half of the war in 300 cases of lung wounds treated medically there was a mortality of from 25 to 28 per cent. By the surgical treatment in cases brought in with severe hemorrhage there were good results in from 65 to 68 per cent. of all cases. By the operative treatment of war wounds of the lung the mortality had fallen from 28 to 9 per cent. Pierre Duval (*N. Y. Med. Jour.*, Dec. 28, 1918).

**EVOLUTION OF PRESENT METHODS.**—A very great change has come over the whole treatment of gunshot wounds. At the beginning of the war, as stated by George E. Gask (*N. Y. Med.*

Jour., Dec. 28, 1918), they were horrified to find that every single wound was suppurating. All efforts to get clean wounds had been futile. They now realized that the essential treatment was early mechanical cleansing by open operation under aseptic precautions before the organisms introduced by the missile had a chance to multiply and invade the tissues. In the majority of cases operation was done within 12 or 15 hours of the time of injury. For the first 2 years of the war they were afraid to do any sort of operation on the chest. The men were put to bed, given morphia if in pain, a remedy for cough if there was cough, and it was hoped they would get well. Quite a large number did, but a larger number died, and a large number became extremely septic, had empyemata with pus discharge. The only surgery that was done was the removal of an inch or 2 of rib and a tube put in. Throughout the time of the Somme fighting they had no time to study these chest cases, for the number of urgent operable cases was enormous.

Gradually they found that the thoracic cases could be divided into 2 categories: those dying on the battlefield or within a few hours, and those dying in from 48 hours to 2 or 3 weeks. In the former class death was the result of hemorrhage; in the latter, usually death resulted from sepsis. The next step was to find the channel of infection, and the principle reached was to effect an early mechanical cleansing of the wound of the chest wall and of the wound in the lung. They put the patient to bed, the chest being examined for complicating wounds, hemothorax, pneumothorax, movements of the diaphragm, position of the heart, and for any indication of respiratory distress. X-ray examination being used when possible. When needed, they cut down upon the rib or scapula, finding it necessary often to excise ragged splinters with a pair of scissors. Very often bleeding was found in the costal artery, which was thought to come from the lung; this was tied. Inserting a finger, there could be felt splinters of bone in the cavity or sticking into the lung. Such cases with the air sucking in and out were uniformly fatal.

Later they were led to enlarge the wound of entrance that the hand might enter the thoracic cavity and remove foreign bodies. To their astonishment, the men stood this much better than was anticipated. It banished the principle that handling of the wounded lung would cause renewed bleeding. On opening the chest the blood was removed and search was made for foreign bodies, examining the lung as in a coil of intestine. If the foreign body had penetrated into the lung a fresh incision might be required. This could be made without fear except near the hilus, and any bleeding was easily controlled by deep catgut sutures. The principle, that a wound must be cleansed, proved true in wounds of the lungs as in any of the soft parts. As evidence of the fact that the lung was able to take care of many organisms without abscess formation; gas gangrene of the lung was unknown in spite of the many cases in which foreign bodies were left in the lung. It was, therefore, a matter of practice to close every wound in the lung. Cleansing of the pleural cavity was of the utmost importance. Closure of the chest was the final step in the operation, and this was done as in closure of the abdomen, when possible—muscle to muscle, and skin to skin.

An anesthetic could be given with safety if there was fair function on the side of the chest not opened. The type of anesthetic was of no great importance so long as it was skilfully given. Probably not more than 30 per cent. of penetrating wounds of the chest should be subjected to operation.

**Indications for early operation:** 1. Such wounds of the soft parts as would require operation in any other part of the body. 2. Bleeding from that wound; intercostal hemorrhage. 3. Fractured ribs. 4. Cases with large foreign bodies lodged in the lung. 5. Cases of pneumothorax in which air was admitted through the wound. In hemothorax without extensive wounds, splintered ribs, or retained bodies, there was at the time diversity of opinion. While they were inclined to operation, their practice was not to operate unless there was some sign of sepsis. Theoretically there should be no such state as

an infected hemothorax; but practically there were a considerable number of such cases. We had no means of telling which cases would become septic. He believed that closure of the chest helped to expand the lung, for every movement aided in this expansion as soon as the air was absorbed. If pus was formed a stitch might easily be removed and a tube inserted. The surgical treatment of wounds of the chest was now being practised in almost every hospital at the front line, and many patients restored to health who would have died under the former treatment.

It must never be forgotten that the man with a bullet in his lungs has a bullet in 2 places—in his lung, and also on his mind. A second operation is often undertaken in order to get rid of the bullet on his mind. The only reliable method of examination is by the X-ray, and for the removal of the foreign body Sir Berkeley Moynihan found that, with few exceptions, an **incision at the level of the fourth rib** offered an easy route of exit. The lung should be handled as gently as possible in searching for the foreign body, and when located it is a simple matter to make an incision and extract it. A stitch is then inserted with a curved needle. It is of great importance not to encourage a too rapid inflation of the collapsed lung. Sir Thomas Myles (N. Y. Med. Jour., Dec. 28, 1918).

Various other details are embodied in the technique described by Lockwood and Nixon (Brit. Med. Jour., Jan. 26, 1918) as follows: Formerly the parietal wound was excised, the comminuted fragments of rib removed, and the pleura, if possible, closed. No attempt was made to clear out the hemothorax, or to follow the missile into the chest. Repair of the thoracic contents was not embarked upon.

In July, 1916, repair of the diaphragm became a routine procedure by the abdominal route. Extensive injuries to the bony skeleton of the thorax were seen to be almost invariably fatal. The principal cause of death was not sepsis. The patients did not recover from the shock and exhaustion of gross bony lesions until the

writers began to remove all comminuted bone and sharp spicules. From this time it became an established rule to operate on the parietes on all "stove in" chests.

An important advance was made when a case was recognized in which the diaphragm was injured by a purely thoracic wound. A successful operation was performed by the thoracic route instead of, as previously, by the abdominal. Thenceforward they adopted the practice of dealing with thoracic injuries of the diaphragm through the thoracic wound.

Up to the end of 1916 open (sucking) wounds of the chest—traumatopnea—had shown a mortality of almost 100 per cent. Various methods of plugging the hole in the chest wall were found to postpone, but not to avert, the fatal result. At this time they realized that it was practicable to excise the parietal wound, clear out completely the hemothorax, and close the opening of the chest wall.

The surgical measures which these cases appear to justify should not be attempted unless: (a) Active resuscitation can be carried out immediately after admission. (b) The services of an expert radiographer are at all times available. (c) The physical signs can be carefully studied and judiciously interpreted. (d) The most perfect asepsis can be secured at the operation.

Given these conditions, they are guided by the following general rules for operation: Operate 1, as soon as the patient's condition allows. (This is much earlier with local than with general anesthesia.); 2, in all cases where injury of the diaphragm is suspected; 3, on all cases with open pneumothorax (traumatopnea); 4, on all badly "stove-in" chests, where the pleura is lacerated, even though there is no external wound; 5, on all cases where a large missile has traversed the pleural cavity, whether lodged in (a) The chest wall, (b) the pleural cavity, (c) the lung, (d) the mediastinum, or (e) the pericardium; 6, on all very acutely infected cases, even though the missile is not retained.

The general mortality of gunshot wounds in the advanced ambulances and in the hospitals of evacuation was on an average 30 per cent., this percentage not taking into account a

large number of deaths which occurred in the advanced posts and in the base hospitals. The writer's statistics from the Battle of the Somme where, excluding operations of urgency, cases were treated medically, show a mortality of 20 per cent. in 300 cases. In a later series when the operative method of treatment was employed, 18 cases were operated out of 118 and no deaths; 100 cases treated immediately with 1 death from empyema. In a total of 136 cases—118 not urgent and 18 urgent—the general mortality was 9 per cent. It will be seen, therefore, that surgical treatment lowers the mortality very considerably. What is more, when septic complications do occur, they are less serious. Surgical treatment of the lung should, therefore, be considered as the logical prophylactic procedure to prevent sepsis. P. Duval (*Surg., Gynec. and Obstet.*, Jan., 1919).

### FOREIGN BODIES IN THE PLEURAL CAVITY, LUNG, AND HEART.

Foreign bodies, bullets, needles, pins, nails, and fragments of iron or other material have not infrequently found a more or less permanent resting place in the pleural cavity, in the lung-tissue, in a chamber of the heart, or in the muscular substance of this organ.

These various bodies enter in many ways, the most common being by violence, as from a gunshot wound, explosion, thrust of a pin or needle, but occasionally they reach their resting place by a process of wandering or ulceration, as when an iron nail is inhaled and finds its way into the pleural cavity, a needle is swallowed and comes to anchor in the pericardium or heart. A case is reported in which a bullet fired into and lodged in the neck was found years afterward in the right ventricle of the

heart, where it apparently remained as an inoffensive body.

Bullets, fragments of bone, pieces of clothing, and drainage tubes have sometimes found their way into the pleural cavity, where they have continued to act as irritants or as infectious objects until removed.

Indications for operation in the later stages of gunshot wounds of the chest are: foreign bodies in the parietes with or without sinuses; foreign bodies in the lung irrespective of size if associated with persistent cough, hemorrhage, or supuration; large foreign bodies in the lung, even if the symptoms are purely nervous; all foreign bodies lodged in the pleura with or without empyema; all cases of infected hemothorax; all cases of through-and-through wounds with shrinking of the side, lessened lung expansion, and interference with movements of the diaphragm in which treatment by exercises, etc., has failed. Turner (*Surg., Gynec. and Obstet.*, Jan., 1919).

The governing principles in the early treatment of gunshot wounds of the chest are the early mechanical cleansing of the wound, both of the chest wall and of the injured viscera, the evacuation of all foreign bodies and of effused blood from the pleural cavity; the repair or suture of the damaged lung and the closure of the chest cavity by suture. Gask (*Surg., Gynec. and Obstet.*, Jan., 1919).

**Diagnosis.**—The presence of a foreign body may be suspected by the history and symptoms presented, and the suspicion may be verified by the use of the Roentgen ray. Unfortunately, sometimes there is no suspicion of the presence of a foreign body until accident, a surgical operation, or a necropsy discloses its presence.

**Treatment.**—Obviously, the ideal treatment is the removal of the



offending body. But there are contraindications, as when the body is encysted and doing no harm, or when the operation for removal is very dangerous. If the patient is already in great danger, or if the situation of the foreign body is such that it threatens life, even a very dangerous operation which offers relief is then justifiable. Tuffier diagnosed, with the Roentgen ray, operated, and removed a bullet which for several months had been imbedded in the wall of the left auricle of a soldier, with recovery of his patient.

The writers report 2 cases of projectiles found lodged in the wall of the heart and well tolerated. In 1 case the projectile, a rifle bullet, was radiologically fixed in the lower narrow part of the left ventricle. In the second case a fragment of shell was similarly demonstrated in the anterior wall of the heart.

Since the beginning of the war 14 cases of this kind have been published. In 7 of these the projectile was lodged in the heart wall and in 7 it was more or less free in a cavity. In 5 of these 14 cases the tolerance was almost perfect. Seven were operated upon, of which 4 recovered and 3 died after operation. In 1 case there was later migration with recovery; 1 died without intervention. Escande and Brocq (*Rev. de chir.*, lii, 268, 1917).

Three cases are reported in which the writer extracted a cardiac projectile successfully. In 2 of the cases the projectile was a rifle bullet, in 1 case encysted in the posterior wall of the left ventricle behind the apex, and in the other case resting on the left auricle. In the third case the projectile was a piece of shell lodged in the posterior wall of the left ventricle under the auriculoventricular ridge. Derache (*Bull. et mém. Soc. de chir. de Paris*, xliii, 1759, 1917).

For the removal of foreign bodies from the pleural cavity and lung the

same principles govern: the case must be studied, the body carefully located by means of the Roentgen ray, and the operation planned so as to accomplish its purpose by following the safest route. The war has greatly augmented our resources in this connection.

In over 200 cases of gunshot injuries of the lungs, early in the war the outcome in cases reaching the base hospitals was surprisingly good. The writer found that the presence of the bullet in the thorax did not seem to influence the clinical course. There was no abscess or gangrene in any of his 56 cases, and there has been nothing so far to indicate that tuberculous processes have flared up under the injury. Toenniessen (*Münch. med. Woch.*, Jan. 19, 1915).

Extraction of metallic foreign bodies from the lung was found by the writer an easy and safe procedure which should be undertaken in all cases, even with a projectile at a depth of 7 cm. in the lung. Prior localization with the X-rays is essential. An incision parallel with the ribs is made over the foreign body, and the nearest rib resected for 4 or 5 cm. The lung is fixed to the thoracic wall by 3 or 4 catgut sutures, a rectangle of lung bounded above and below by ribs and laterally by the cut extremities of the resected rib being thus attached. After incision of the lung, the finger is pushed directly into it. Foreign bodies are readily felt, even at a distance. The lung is either torn through with the finger, or the tissue containing the foreign body drawn toward the wound with Kocher forceps and the body removed with grooved director or bistoury. A tampon with strong phenol is then inserted directly into the pulmonary tissue and an ordinary dressing applied. In none of 26 cases did more than a little cough and bloody expectoration follow the procedure. Complete healing in 2 to 4 weeks uniformly followed. G. Marion (*Presse méd.*, Sept. 16, 1915).

The writer refers to the recent report of Marion in which he relates the extraction of intrapulmonary projectiles from 27 wounded men by a simple operatory technique and without any subsequent mishap. Over 100 cases of penetrating gunshot wounds of the chest showed the writer that habitually there is good tolerance of intrapulmonary projectiles. Moreover, every penetrating chest wound with or without lodgment of a projectile is characterized by the simultaneous production of a pneumonic process and a hemothorax. The essential fact which the surgeon should note is that there is a slow resolution of this pneumonia and a slow resorption of the hemothorax. This slow evolution is observed whether or not there is a retained projectile. Such clinical showings warn that patience and abstention should be observed until such time as a spontaneous recovery is effected. Two complications, pulmonary abscess and persistent hemoptysis, appear to the writer to clearly indicate operations. These complications are generally very rare, the first having been observed by him only twice in over 100 cases and the second not at all. Piery (*Presse méd.*, p. 274, 1916).

Fifteen cases illustrated the facility of operative extraction of a projectile in lung tissue causing pain and dyspnea. The writers proceed by preliminary **fixation of the lung**, when it is free, if not, by systematically **inducing pneumothorax**, their experience having confirmed the harmlessness of pneumothorax when it develops slowly. Desgouttes and Perrin (*Lyon chir.*, July-Aug., 1916).

Extraction under screen control of projectiles in the lungs was performed by the writer in 97 cases and by others 200 times for the extraction of 230 projectiles in lung tissue. All but 1 of the men recovered promptly and resumed their military service. A blunt instrument worked slowly into the parenchyma of the lung does not injure it, provided it keeps to a straight path and does not

enter the hilus region. The cottony elasticity of the pulmonary parenchyma, the blood-vessels and air vessels, enables them to automatically yield the way to the rounded tip of the instrument, and allow it to pass without injuring them. The projectile is located beforehand by having the man stand with his arms over his head, and slowly turn around before the screen. The displacement of the shadow during rotation soon locates the projectile with precision. For the operation the anesthetized man lies on a frame that pivots on its longitudinal axis to apply this rotation principle at need.

The patient is placed under the screen, the tube is below; a button-hole incision made over the foreign body, and a closed extracting forceps introduced and pushed in obliquely until it reaches the body. The forceps is then opened and the body seized and extracted. Neither pneumothorax nor hemothorax follows. The narrow, blunt tipped forceps must be introduced slanting, through sound tissue. The danger points are the intercostal veins and the hilus. When the projectile is in the hilus, **thoracopneumotomy** is preferable. The writer has performed 730 operations for extraction of foreign bodies under screen control, switching on and off the X-rays at will, alternating them with a bright orange-red light. He regards this economical radio-operative technique as a great advance as it avoids all useless mutilation. De la Villéon (*Jour. Amer. Med. Assoc.*, from *Presse Méd.*, May 31, 1917).

**Pericardiotomy** was performed by the writers on the 12th day after passage of a rifle bullet through the chest, with recovery. Noble and Vine (*Lancet*, Jan. 18, 1919).

Direct inspection of the bronchi by means of the bronchoscope renders direct removal possible when the foreign body has not reached much beyond the trachea in the first bronchial segments.

## WOUNDS OF THE THORACIC DUCT.

Wounds of the thoracic duct occur most frequently in the course of operations on the left side of the neck behind the inner end of the clavicle. Operations on the right side of the neck may also injure the thoracic duct, as it sometimes divides, one branch passing to each side of the neck, to empty into the subclavian vein at its junction with the internal jugular. The thoracic duct often empties into the vein by means of two or more ducts, so that the obliteration of one or even two ducts may have no serious result. The right lymphatic duct, which receives the lymph-vessels from the right side of the head and neck, right upper extremity, right lung, etc., also sometimes empties by two or more branches into the right subclavian vein at its junction with the internal jugular, and may be injured by operations on the right side of the neck. Besides these points of communication with the venous system, the thoracic duct or its branches have other points of communication, as with the azygos and other veins—facts important to remember as explaining recovery after obliteration of important branches. The thoracic duct or its branches may also be injured—crushed, cut, or ruptured in the abdomen or in the thorax.

**Symptoms.**—When a large lymph trunk is opened, the escape of lymph is sufficient evidence of the injury. In concealed injuries, however, as in the abdomen or thorax, the symptoms are more obscure. There may be weakness, thirst, fever, rapid pulse, and an accumulation of fluid in the peritoneal or pleural cavity, or

in the connective tissue outside of the serous sacs. On aspiration the nature of the fluid is recognized and its source may then be surmised.

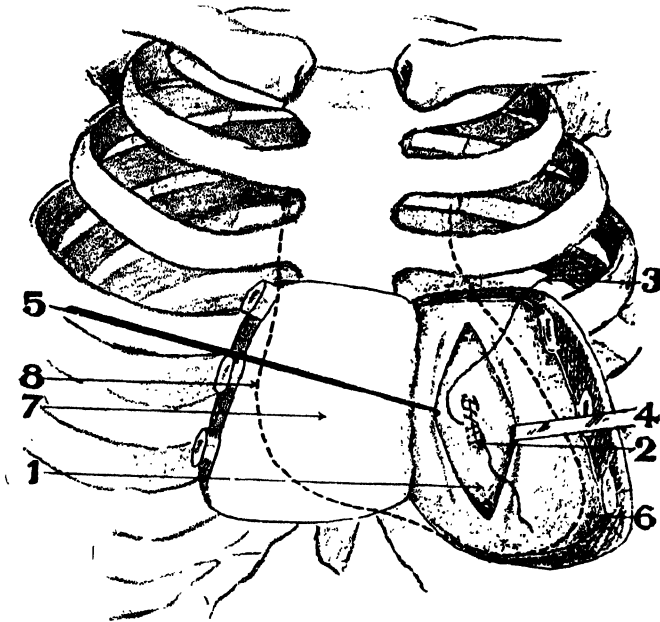
The **prognosis** of wounds of the thoracic duct seems to be very good. Of 22 cases reported by Lécène, there was only one death and that was due to sepsis.

**Treatment.**—If during an operation about the neck a milky fluid suddenly appears, its flow should be arrested by pressure until search is made for the wounded duct. If this can be found and if other branches opening into the vein can be found the wounded duct should be ligated. If the ends of the severed duct appear they may be sewed together or anastomosed with a convenient vein. Often it is impossible to find the vessel, and packing with gauze must be depended on to stop the leak. The patient should be kept quiet and the fluids somewhat restricted. For accumulations of lymph or chyle in the tissues or cavities, nothing is necessary unless pressure symptoms become serious—then the fluid should be partially or completely withdrawn by aspiration.

Study of 58 cases in literature and a personal case. The accident occurred during operation for tuberculous lymph-nodes in the neck in 18 cases, for cancerous in 13; in 9 cases for removal of a tumor in the neck, and once for an aneurism. It can be treated by tamponing, by ligation or clamping, by suture, or by implantation of the injured duct in a vein. Of the 21 patients treated by tamponing, 3 died, and in 14 others there was a persisting fistula. Only in 4 cases was the effect permanent. When the injured duct was closed with a clamp or ligated, the result was good in 9 of the 13 cases in which this was done. In the other

cases there was oozing of lymph, but this gradually subsided, and no harm was apparent from the procedure in any instance. The wound should be sutured as the routine procedure, and ligation should be applied only when it is impossible to suture. No injury from the suture has been observed to date; thrombosis does not have the same importance in this duct as in a blood-vessel. D. G.

out of 40 cases the duct has two terminal branches, it may be expected that ligation of the thoracic duct may be successful in nearly half the cases met with. The surgeon should therefore look for a second terminal branch, and if found, ligation should be carried out. 4. *Tamponade*. This last procedure should be the last resort. The hope here lies in the possibility of establishment of collateral



Operation for wound of the right ventricle of the heart. 1, heart; 2, deep sutures; 3, superficial sutures; 4 and 5, retractors on pericardium; 6, left pleural space; 7, flap of chest wall, including fourth, fifth, and sixth ribs; 8, heart outlined by broken line. (Author's case.)

Zesas (Deut. Zeit. f. Chir., Jan., 1912).

The 4 most available methods of treatment in the order of their relative importance, are as follows: 1. *Suture*. Where this can be accomplished, suturing the wound of the duct is by far the most preferable procedure. 2. *Implantation into a vein*. This should be, by all means, accomplished if the duct is single. Obviously this entails a great deal of technical skill, but the result, if successful, is well worth all efforts. 3. *Ligation of the duct*. Since Parsons and Sargent have shown that in 18

circulation. Edward Harrison (Brit. Jour. of Surg., Oct., 1916).

## WOUNDS OF THE HEART.

The chief wounds of the heart are stab and gunshot wounds.

**Symptoms.**—Hemorrhage is usually copious, but it may be very slight and little blood may appear externally, while in the mean time it is accumulating in the pericardium or pleural cavity. The heart sounds may be feeble, muffled, or have a splashing sound. Increased area of

dullness may be seen in case the blood accumulates in the pericardium. The usual symptoms of severe hemorrhage occur, such as rapid, feeble pulse, restlessness, thirst, dyspnea, sighing respiration, fits of syncope, and blindness.

The tolerance of the heart to injuries has recently been emphasized in many instances. In a soldier treated by Grand-gérard (Paris méd., Jan. 13, 1917) a shrapnel ball entered at the shoulder. Radioscopy showed that it had entered and lingered in the right auricle and passed thence into the inferior vena cava and the femoral vein, finally lodging in the hypogastric vein, all without inducing any appreciable symptoms. Again, under the radioscopic screen Lobligeois (Bull. de l'Acad. de méd., lxxvi, 364, 1916) detected a bullet in the left ventricle. Its movements corresponded with each cardiac pulsation; at the end of the diastole the bullet rested on the lower border of the heart near the apex, then at systole it moved rapidly from left to right. The patient had recovered, and was in no way being disturbed by the foreign body. A similar case was reported by Silvan (Riforma Med., xxxii, 297, 1916). Leriche (Brit. Med. Jour., Oct. 4, 1916), referring to the fact that a man had lived 3 hours after a machine gun bullet had pierced the left ventricle of the heart, the left lung, and produced a vast hemothorax, pointed out that in wounds of the heart death was immediate only in 1 out of 6 cases. The bullet may excite reflex and other distressing symptoms, and yet not menace life. In a case observed by Glaser and Kaestle (Münch. med. Woch., May 25, 1915) the left arm was impotent, and the patient could not breathe normally when lying on either side. He also complained of stabbing pains in the left side, radiating from the costal arch to the shoulder and arm, sharper after eating, keeping up for about an hour. In a man in whom a bullet had penetrated the pericardium, Armstrong (Annals of Surg., June, 1914) observed auricular fibrillation, though no previous inflammatory mischief or symptom of cardiac involvement had

previously existed. Cessation of the disordered rhythm followed removal of the bullet.

**Treatment.**—If there has been a wound of the cardiac region and the symptoms are threatening to life, an exploratory operation should be resorted to *at once* and the operator be prepared to repair the injury to the heart.

[*Study of the Table.*—The features presented by the table (pp. 146 to 154) may be studied as follows:—

*Time Between Receipt of Wound and Operation.*—In 106 cases this time is given all the way from “at once” to five days—the large majority of patients, 88, being operated on not later than six hours after the injury (44 in one hour or less and 44 in from any time over one hour to six hours), with 35 (39.75 per cent.) recoveries; 10 between six and twelve hours, with 5 recoveries; 1 between twelve and eighteen hours, with recovery; 4 between eighteen and twenty-four hours, with 1 recovery; 2 between twenty-four and forty-eight hours, with 2 recoveries, and 1 after five days, with recovery. These figures would indicate that, the longer the time after injury before operation, the less the mortality, but it must be borne in mind that in the worst cases the patients die or are saved by operation before the expiration of the first six hours, and those who survive this time are the best risks from an operative standpoint.

*Location of External Wound.*—Ever since Joab so treacherously and fatally smote Amasa in the fifth rib a wound in this region has been regarded as especially dangerous, and the figures here presented confirm this opinion. Of 133 patients in whom the situation of the external wound was given, 130 were on the left side, including: 1 through the first intercostal space; 6 through the second intercostal space; 19 through the third intercostal space; 52 through the fourth intercostal space; 36 through the fifth intercostal space; 7 through the sixth intercostal space; 2 through the seventh intercostal space; 6 below the costal cartilages.

On the right side there was 1 case each of wounding through the second, fourth, and fifth interspaces. Ninety-one, or 68 per cent., were just above or just below the fifth rib, and 110, or 83 per cent., were between the third and the sixth ribs.

*Instrument by which Wound was Inflicted.*—Of 140 cases in which the weapon was indicated, 117, or 83 per cent., were caused by knives or poniards; 16, or 12 per cent., by bullets; 2 by scissors; 2 by iron pickets; 1 by a fragment of glass; 1 by a needle, and 1 by a sharp-pointed body. In 10 the instrument is not given. VAUGHAN AND WILLSON.]

### Method of Exposing the Heart.—

No single method has yet been agreed on as the best. The kind of operation is often determined by the external wound, and, begun as an exploration; the subsequent steps depend on the necessities which arise during its progress. This probably accounts for the large number of resections of cartilages or parts of ribs rather than the formation of a well-planned flap of skin, muscle, and ribs.

The human heart is even more tolerant of surgical manipulation than that of the cat or the dog. Local anesthesia or paravertebral nerve blocking with a 1,  $\frac{1}{2}$  or  $\frac{1}{4}$  per cent. **novocaine** solution is to be preferred for the chest wall. At times an associated moderate narcotism with **scolamine-morphine** is desirable, or a slight ether narcosis, to be preferred where haste is essential. A shocked, semi-unconscious patient may require no anesthetic. If the pleural cavities are to be invaded, **intratracheal insufflation** after the method of Meltzer-Auer has advantages. To restrict the action of the vagus, a preliminary injection of **atropine** may be given subcutaneously, while **cardiac massage** and the intravascular injection of **adrenalin**, avoiding any excess, are most valuable methods in starting the arrested heart. Gunshot wounds have been found more dangerous than incised wounds. W. Wayne

Babcock (N. Y. Med. Jour., June 10, 1916).

The best method is one that will freely expose the heart and not open the pleura or leave the chest wall permanently impaired. The chief methods are:—

(a) *The Operation Through an Intercostal Space.*—In a long chest with wide spaces this may be done. Somerville reports a successful suturing of the left ventricle through the

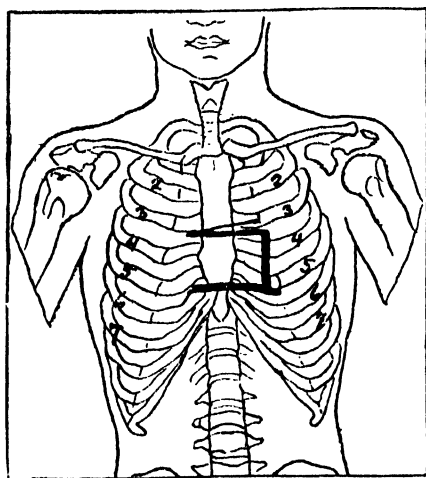


Fig. 1.—Flap of sternum and cartilages of fourth and fifth ribs; hinge on the right. (H. Lorenz and others.)

fourth intercostal space. This method may be modified and the space increased by the division of one or two cartilages.

(b) *Resection of One or More Cartilages With or Without a Portion of Rib.*

(c) *Flap Method Across the Sternum* (H. Lorenz and Others; Fig. 1).

—A transverse incision is made from the right side of the sternum in the third intercostal space across the sternum to the left chondrocostal junction, and, then, a corresponding incision in the fifth intercostal space across the sternum. The left ends of

these incisions are then united by a vertical one. The sternum and cartilages are divided with bone forceps along these incisions after ligating the internal mammary arteries, and the flap formed is turned to the right,

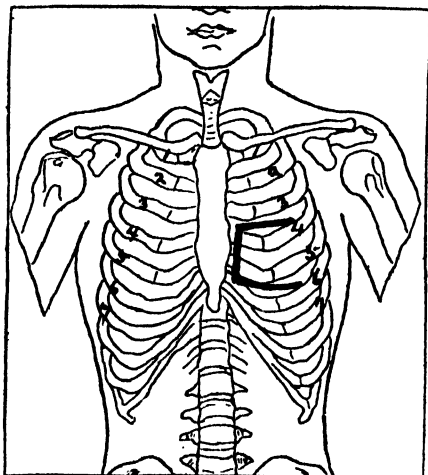


Fig. 2.—Flap of the fourth and fifth ribs and their cartilages; hinge external.

making a hinge of the right chondrosternal joints. This exposes the heart well and avoids opening the pleura.

(d) *Flap of Cartilages and Ribs, Hinge External* (Fig. 2).—In this method the fourth and fifth cartilages are divided near the left border of the sternum; the third and fifth inter-spaces are divided laterally nearly or quite to the nipple line. The flap is raised by its inner border, the pleura stripped off if practicable, and the ribs are broken or cut near the costochondral junction.

(e) *Flap of Cartilages and Ribs, Hinge Internal* (Fig. 3).—This method is just the reverse of the preceding, the trap-door opening near the left nipple line and hinging on the left fourth and fifth chondrosternal articulations. The pleura is probably always opened in this method. If more

room is needed or the location of the external wound requires it, the flap may include additional cartilages, above or below. The last two methods can be quickly performed and expose the heart well, but are almost certain to open the left pleura. Of 133 operations, in 60 a portion of one or more cartilages or ribs were resected; in 71 a flap of the chest wall was made with the hinge external or internal—occasionally the hinge was placed above or below, and in 2 cases the suturing was done through an intercostal space.

[Of 142 patients the left ventricle was wounded in 68, the right ventricle in 68, the left auricle in 4, the right auricle in 4; 2 had each 2 cavities wounded (1 both ventricles and 1 the right auricle and right ventricle), and in 8 the cavity is not mentioned or the weapon passed between 2

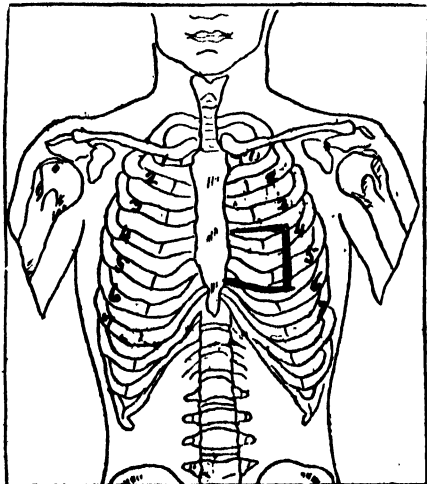


Fig. 3.—Flap of the fourth and fifth ribs and their cartilages; hinge internal.

cavities. These statistics show that the two sides of the heart are equally liable to injury, but that the ventricles are in much greater danger than the auricles in the proportion of 17 to 1.

The size of the wound in the heart varied from 0.5 cm. ( $\frac{1}{2}$  in.) to 6 cm. ( $2\frac{1}{4}$  in.). In every case the wound was

sutured. The favorite suture material was silk, but catgut was used in many patients. Continuous and interrupted sutures were both used and were introduced by most operators whenever convenient, regardless of systole or diastole. It seems to make no trouble if the suture does enter the cavity of the heart. Tumultuous heart action sometimes interfered with the introduction of the sutures. This was overcome by holding the heart in one hand or using one or two deep sutures, "tension sutures," by which the heart was steadied or drawn forward as might be necessary. In several cases heart massage was used in order to revive a pulseless heart and in a few cases the heart resumed its function.

*Drainage of Pericardium and Pleura.*—In 46 patients the pericardium was drained, with 25 recoveries and 23 deaths; in 44 the pericardium was not drained, with 25 recoveries and 19 deaths; in 42 both pericardium and pleura were drained, with 21 recoveries and 21 deaths; in 19 both pericardium and pleura were closed without drainage, with 12 recoveries and 7 deaths; in 72 the pleura was drained, with 30 recoveries and 42 deaths; in 21 the pleura was not drained, with 13 recoveries and 8 deaths. VAUGHAN AND WILLSON.]

The lesson taught by the above is to do away with drainage. Some of the disadvantages of drainage are the risk of secondary infection, irritation or inflammation excited by the gauze or tube, and the bad effects on the collapsed lung of keeping the pleura open. However, some cases should be drained, as when infection is highly probable or hemostasis has not been satisfactory.

[Of 150 patients operated on, 98 died and 52 recovered, a mortality of 65 per cent., about the same as it was twelve years ago and in 1901, when 26 cases were reported. Naturally, the mortality must always be high. Thirty-two patients died in less than twenty hours after operation or the reception of the wound, 15 on the operating table during or just after operation—nearly all from loss of blood, though 1 death was attributed to pneumothorax

on opening the left pleura. Thus 32, or 20 per cent., of the patients are moribund when the surgeon first sees them.

The remaining 66 deaths occurred from twenty-four hours to five months after operation; 6 of pleurisy, 5 of pericarditis, 21 of pleurisy and pericarditis together, 3 of pneumonia, 3 of peritonitis, 2 of pericarditis and nephritis, 1 of pleurisy and cerebral abscess, 1 of pleurisy and wound of the tricuspid valve, 1 of pleurisy and double pneumonia, 1 of gangrene of the lung, 1 of two wounds of which one was not sutured, 3 of hemorrhage in the pleura, 2 of hemorrhage in the pericardium, 1 of clot in the tricuspid valve, and in 15 the cause is not given.

We see that 44 of those who died after the first twenty hours, or 86 per cent. (omitting the 15 in which the cause of death is not given), died of infection, and of the 52 who recovered only 12 escaped without infection, 22 had pericarditis or pleurisy, and in 18 it was not stated. Of the entire 118 patients surviving the first twenty hours, 62, or 52 per cent., suffered from infection.

The mortality with reference to the cavity wounded is as follows: 68 of the left ventricle, with 42 deaths, or 62 per cent.; 68 of the right ventricle, with 48 deaths, or 70 per cent.; 4 of the left auricle, with 2 deaths, and 4 of the right auricle, with 1 death.

Sixteen gunshot wounds were operated on, with 9 deaths and 7 recoveries, a mortality of 56 per cent. In the 134 cases with other wounds 89 died and 45 recovered—mortality 66 per cent., from which it would appear that gunshot wounds of the heart have about 10 per cent. lower mortality than other kinds of heart wounds. VAUGHAN AND WILLSON.]

On the whole, it may be concluded that there is no longer any question as to the propriety of the **operation**, since 35 per cent. of the patients recover, compared with 15 per cent. (according to Holmes and Fisher, 1881) of recoveries after non-operative treatment—a gain of 20 per cent.

The mortality is practically the



same as it was when the operation was first introduced, and it behooves the surgeon to study the matter and find a means of improvement.

The two great causes of death are hemorrhage and inflammation of the pleura or pericardium. Probably little more can be done than has been done to prevent death from hemorrhage, but, inasmuch as more than half the patients who survive twenty hours have infection, great attention should be given to the prevention of this complication.

There is room for great improvement in preventing infection. Besides the observance of strict asepsis the question of opening the pleura and of drainage of pleura or pericardium acting as predisposing causes of infection is of the greatest importance.

Sepsis is the common cause of failure. This is in part due to the difficulty of preparing the patient for the operation with the same thoroughness as in cases less urgent, but chiefly to the fact that the injury is inflicted with a dirty (septic) instrument or weapon, and if the pleura is injured, as is so commonly the case, air and germs have free access to the parts. Bland-Sutton (*Brit. Med. Jour.*, May 28, 1910).

As a rule, therefore, the pericardium and pleura should not be drained.

The advisability of **early removal** is suggested by a case of the writers', in which syncope and dyspnea after exertion, severe palpitations, and a constant sensation of constriction and oppression in the chest, led to extraction of the bullet 6 months after the injury. Scraps of cloth were found in its bed in the auricle wall. Couteaud and Bellot's (*Revue de chir.*, Dec., 1915).

To **extract missiles** from the heart and pericardium the writer exposes

the anterior and lateral aspects of the heart, and makes a horseshoe flap of skin and muscle with its pedicle over the sternum. Portions of the second, third, fourth, or fifth cartilage are resected and the pleura covering the heart detached and reflected outward. Where the foreign body is located posteriorly, access, as in the anterior cases, is obtained by 1 or 2 costal cartilages, from the second to the fifth, followed by a lateral incision 2 or more cm. long on the lateral aspect of the pericardium, thus exposing the posterior pericardium and posterior cardiac surface. O. Laurent (*Bull. de l'Acad. de méd.*, Nov. 30, 1915).

The writer **extracted** a piece of shell from the right ventricle. The latter was caught between 2 fingers and pulled forward, incised, and the piece of shell removed by forceps; some black blood escaped, but a few catgut sutures produced hemostasis. The pericardium was **sutured**. The condition appeared to progress satisfactorily for more than a week. On the 13th day after operation signs of pericarditis appeared, which proved fatal. Richat (*Bull. et mém. Soc. de chir. de Paris*, xlii, 1100, 1916).

The writers report 2 cases of shell wound of the heart with almost immediate operation and recovery in both. The first was a case of deep but non-perforating injury of the left ventricle. The **missile** was **removed** from the pericardial sac, the **wound sutured**, and the patient discharged on the fifteenth day. In the second case, an opening sufficiently large to admit a lead pencil had been produced in the left auricle. Suture was successfully effected, but the subsequent course of the case was complicated by a left sided infected hemothorax. Sterilization of the pleural cavity was accomplished with **Dakin's fluid** and the patient discharged after 7 weeks, the X-rays showing the shell fragment still embedded in the left lung. Constantini and Vigot (*Presse méd.*, Nov. 29, 1917).

Following is the bibliography, arranged alphabetically by publications, and the table, arranged alphabetically by operators, with year of operation as nearly as ascertainable, and with figures of reference to the bibliography. (See page 146.)

Case of bullet wound of the heart, lung, and liver operated on six hours after the injury, when the patient was almost moribund. An opening was found in the left ventricle and **sutured**. Although hemorrhage was completely arrested, the patient died before the operation was finished. From a study of the subject the authors conclude that heart wounds rarely exist without pleural or lung involvement. Operative rather than expectant treatment is indicated in a large proportion of the cases. Osteoplastic flaps should not be employed. Intercostal incision, with or without subsequent division of ribs, is the preferable method of approach. In certain cases the heart wound may be of sufficient size to permit violent hemorrhage at the time of suture. In these, interrupted manual compression of the superior and the inferior cavæ may be a possible safe procedure; the profuse hemorrhage without this compression is of greater danger. Differential pressure with apparatus is by no means a *sine qua non* in all operations for wounds of the heart and lungs. It is, however, a valuable agent to control the respiratory function, to regulate the heart beat, and to reinflate the lung at the end of the operation. Airtight closure of the pleural cavity with reinflation of the lung should be employed when possible; the intercostal incision followed by a pericostal stitch is a successful method of securing tight closure. G. W. W. Brewster and S. Robinson (Annals of Surg., March, 1911).

The small bullet was found close to the sternum of the boy of 8 about an hour after the accident. The grave symptoms indicated hemorrhage in the pericardium but not a

trace of perforation of the pericardium could be found. Nevertheless the pericardium was opened with a Y-incision and the apex of the heart brought out. A jet of blood suddenly spurted nearly 70 cm. high, but was arrested with the left thumb and finger. With the right hand an **X suture** was taken in the myocardium and the heart was replaced. The interest of the case lies in the injury of the heart with no signs of perforation of the pericardium. The heart seems perfectly normal now. L. Vaccari (Polieclinico, Feb. 24, 1918).

The prognosis of immediate operation in heart wounds is reviewed by the writer. He quotes Hesse as collecting from literature 70 recoveries in 160 operations for stab wound of the heart and 12 recoveries in 27 gunshot wounds treated by immediate operation. He believes that one can count on about 45 per cent. of recoveries in heart wounds. The shorter the time between injury and operation the better the prognosis. Hesse says that in operations made during the first 4 hours the mortality should be no higher than 25 per cent. Wounds of the pericardium cause hemorrhage with accumulation of blood in the pericardial sac, causing pressure upon the heart and symptoms very like those of injury of the heart itself. Treatment consists in **removal of the blood and ligation of the bleeding vessels**. In cases seen several days after injury the blood may be removed by **paracentesis**. Plus in the pericardial sac demands ample **drainage**. J. R. Eastman (Med. Record, Feb. 16, 1918).

Case in which necropsy revealed that a prompt operation might have saved life. The bullet had penetrated the outer pericardial layer, but the inner had stretched without rupturing. The distended ventricle was ruptured by the bullet, still driving the inner pericardium before it. The writer found 16 similar cases on record, some with recovery. R. de J. de Jong (Nederl. Tijdsch. v. Geneesk., Jan. 18, 1919).

TABLE OF RECORDED CASES OF SUTURE OF THE HEART.

No. Operator and Year of Operation.	Time between Wounding and Operation. Anesthetic.	Location of External Wound and Instrument by which Inflicted.	Method of Exposing the Heart.	Cavity Wounded and Treatment.	Drainage of		Complications.	Result.
					Peri-cardium.	Pleura.		
1 Alves de Lima 39 1906	Soon. Chloro.	Knife cut over fourth cartilage.	Flap of 3rd and 4th ribs; hinge external.	L. V.; 14 mm.; 1 catgut suture.	No.	Yes.	Mitral valve wounded. Heart stopped twice and was revived by massage.	Died one hour later. Hemorrhage.
2 Baliva 37 1897	.....	Stab wound of heart.	.....	Heart wound sutured.	....	....	.....	Died quickly.
3 Bardenheuer 37 1904	.....	Gunshot wound.	.....	Heart perforated; entrance and exit wounds sutured.	....	....	Pericarditis and pleuritis.	Died 2 days later.
4 Bardenheuer 37 1904	.....	Stab wound.	.....	.....	....	....	Pericarditis and pleuritis.	Died 10 days later.
5 Barth 1901	1/4 hr. Chloro.	Knife cut through the ensiform cartilage.	Resection of right 5th, 6th and 7th cartilages.	R. V.; 2 cm.; 4 silk sutures.	Yes.	Yes.	Right pleura and tricuspid valve wounded.	Died on fourth day; pleuritis.
6 Barth 1901	1/4 hr. Chloro.	Knife cuts 3. in fourth left space—3 cm. from the sternum.	Flaps of sternum and left 4th and 5th cartilages; hinge on right.	L. V.; 0.5 cm.; 3 silk sutures.	No.	Yes.	.....	Recovered.
7 Barth 1902	1 hr.	Knife cut 3 cm. within and below left nipple.	Resection of 5th and 6th cartilages.	R. V.; 0.75 cm.; 5 sutures.	No.	No.	Pleuritis.	Recovered.
8 Baudet 24 1906	None. 1 hr. Chloro.	Stab wound in fifth left space 2.5 cm. within and 1 cm. below left nipple.	Flap of ribs; hinge external.	R. V.; sutured.	No.	No.	Pleuritis.	Recovered.
9 Blake, J. A. 1907	2 1/2 hrs. Ether.	Knife cut through fourth left cartilage 1 cm. within nipple line.	Flap of 3rd, 4th and 5th cartilages; hinge internal.	R. V.; 1 cm.; 3 interrupted silk sutures; mattress suture over them.	No.	No.	Pleuritis.	Recovered.
10 Borchardt 27 1904	2 1/2 hrs.	Boy fell from tree and was impaled on iron picket fence.	Incision over 5th rib.	L. V.; 1.5 cm.; on posterior side; 4 silk sutures.	No.	Yes.	.....	Recovered.
11 Borzymowski 90 1902	None.	Knife wound between ensiform and left costal cartilages.	Wound enlarged—resection of 4th, 5th and 6th ribs.	L. V.; apex; 2 cm.; 3 deep and 3 superficial silk sutures.	....	....	Pericarditis and pleuritis.	Died 2 days later.
12 Borzymowski 90 1903	Ether.	Wound over fifth left cartilage.	.....	3 wounds; silk sutures.	....	....	Pleuritis; discharge of silk sutures.	Recovered. Re-section of third rib 2 mos. later for empyema.
13 Borzymowski 90 1903	Ether.	Knife cuts 2. over fourth left cartilage.	Flap of ribs, 3rd, 4th and 5th; hinge external.	R. V.; sutured.	....	....	Pericarditis and pleuritis. Two wounds, only one sutured.	Died 2 days later.
14 Bougle 1901	1/4 hr. Chloro.	Pistol ball in third left space; a finger's breadth from the sternum.	Flap of 3rd, 4th and 5th cartilages; hinge external.	R. V.; 2 holes; both sutured with catgut.	No.	Yes.	Ball had passed through wall of ventricle not opening cavity. Wadding in wound.	Died 5 hours later.
15 Brachini 1901	None.	Knife cut in fourth left space; 3 cm. outside nipple.	Flap of 2nd, 3rd, 4th and 5th ribs; hinge external.	Interventricular groove; 5 silk sutures.	....	Yes.	Pericarditis and pleuritis.	Died 1 1/2 hours later.

16 Brachini 1901	At once. None.	Three poniard stabs in region of heart.	Flap of 3rd, 4th and 5th ribs; hinge in- ternal.	L. V.; 2 wounds; 1 non-penetrating; both sutured.	....	....	....	Died on table.
17 Brenner 1901	Next day.	Knife cut over sixth left cartilage.	Flap of 3rd, 4th and 5th ribs; hinge ex- ternal.	R. V.; 7 mm.; sutured.	....	....	Heart muscle de- generated.	Died on table.
18 Brezard and Morel 15 27 1905	Soon. Chloro.	Pistol ball (8 mm.) in third left space 2 cm. from sternum.	Flap of 3rd, 4th and 5th ribs; hinge ex- ternal.	L. V.; 2 wounds; en- trance and exit su- tured with catgut.	No.	....	Cavity of ventricle not opened.	Died on table; hemorrhage.
19 Bufnoir 1899	.....	Gunshot wound in fifth left space; .22 caliber.	.....	R. V.; 1 opening su- tured.	....	....	Ventricle perforated. Exit wound not sutured.	Died.
20 Camus 23 1905	About 1 hr.	Poniard stab in fourth left space, a finger's breadth from ster- num.	Flap of 3rd, 4th and 5th ribs; hinge ex- ternal.	R. V.; 1 cm.; sutured with catgut.	Yes.	Yes.	Left pneumonia.	Died 22 hours later.
21 Camus 23 1905	1 hr.	Knife cut in third left space.	Flap of 3rd, 4th and 6th ribs; hinge with catgut.	5th R. V.; 15 mm.; sutured	....	....	.....	Died on table.
22 Cappelen 1896	1 hr. Ether.	Knife cut in fourth left space; midaxillary line.	Resection of 3rd and 4th ribs.	L. V.; 2 cm.; sutured.	....	....	Coronary art. found cut; was ligated.	Died 3 days later of pericarditis.
23 Capello-Cimoroni 23 1904	None.	Stab wound in seventh left cartilage at margin of sternum.	Resection of 4th, 5th, 6th and 7th ribs.	R. V.; 8 sutures; wound of abdomen.	Yes.	....	Heart sutures dis- charged in pus 15th day.	Died 2 months later; pericardi- tis and sub- phrenic abscess.
24 Carmelo, F. 32 1904	Chloro.	Knife wound in fourth left space.	Resection of 4th and 5th cartilages.	L. V.; silk sutures.	....	Yes.	Bronchopneumonia.	Died 3 days later.
25 Carnabel 1900	2 hrs. Ether.	Knife cut in third left space 3 cm. from ster- num.	Resection of 4th and 5th cartilages.	R. V.; 2 cm.; 3 catgut sutures.	Yes.	Yes.	Pericarditis and pleu- ritis.	Died 4 days later.
26 Dolsetti 27 1906	1 hr. Eucain.	Knife wound in fifth left space without nipple line.	Resection of 4th and 5th cartilages.	R. V.; 1.5 cm.; 3 silk sutures.	No.	Yes.	Heart stopped; re- vived by massage.	Died 7 days later. Peritonitis and mediastinitis.
27 Durante 37 1897	.....	Wound in heart region.	.....	R. V.; sutured.	....	....	.....	Died some days later.
28 Duval 24 1906	.....	Knife cut in fifth left space, 8 to 10 cm. from sternal border.	Flap of 4th, 5th and 6th ribs; hinge external.	L. V.; 1.5 cm.; 2 in- terrupted sutures.	....	....	Heart stopped; warm salt solution in- jected into L. V.; it beat. Cold solu- tion injected and heart suddenly stopped.	Died on table.
29 Farina 1886	Chloro.	Knife cut at upper bor- der of sixth left rib near sternum.	Resection of 5th, 6th and 7th cartilages.	R. V.; 6 mm.; 3 silk sutures.	No.	....	Bronchopneumonia.	Died 5 days later.
30 Fischer, E. 80 1907	1 hr. Ether.	Knife cut in third left space; another over second rib.	Wound enlarged; excision of 3rd and 4th cartilages.	ex-L. V.; silk sutures; coronary vein ligated.	Yes.	Yes.	Pericarditis.	Died 30 hours later.
31 Fontan 1900	6½ hrs. Chloro.	Six scissors wounds be- tween third and seventh left ribs.	Flap of 4th, 5th and 6th ribs; hinge external.	L. V.; 12 mm.; contin- uous catgut sutures.	No.	No.	Pleuritis.	Recovered.
32 Fontan 1901	2 hrs. Chloro.	Knife wound in fourth left space, 0.5 cm. out- side nipple.	Flap of 4th, 5th and 6th ribs; hinge external.	L. V.; 6 mm.; contin- uous catgut sutures.	No.	No.	Pleuritis and em- boli in right lung.	Died 5 months later from brain abscess.
33 Fourmestroux, de 17 21 27 1905	½ hr.	Knife cut a finger's breadth outside 13th nipple.	Flap of 3rd, 4th and 5th ribs; hinge in- ternal.	L. V.; 3 silk sutures.	....	Yes.	.....	Recovered.

No. Operator and Year of Operation.	Time between Wounding and Operation. Anesthetic.	Location of External Wound and Instrument by which Inflicted.	Method of Exposing the Heart.	Cavity Wounded and Treatment.	Drainage of Pericardium.	Pleura.	Complications.	Result.
34 Fourmestroux, de 21 25 1905	10 mins. Chloro.	Knife cut in fourth left space.	Flap of 3rd, 4th and 5th ribs; hinge internal.	L. V. and R. V.; interventricular groove; 3 silk sutures.	....	....	Necropsy. Both ventricles opened by wound through septum.	Died on table.
35 Fummi 1898	Some hrs. Slight.	Knife cut under nipple.	Resection of 5th rib.	L. V. and apex non-penetrating; 1 stitch.	....	....	Pleuritis.	Recovered.
36 Gaumet 23 1906	1 1/4 hrs. Chloro.	Knife cut in fifth left space 5 cm. from median line.	Flap of 3rd, 4th and 5th ribs; hinge external.	R. V.; 4 mm.; 3 catgut sutures.	Yes.	Yes.	Clot found in tricuspid valve; probable cause of death.	Died 24 hours later.
37 Gentil, F. 27 33 53 68 1901	10 hrs. Chloro.	Wounds 3, in fourth left space.	Flap of 5th and 6th cartilages; hinge internal.	L. V.; 1 cm.; sutured with silk.	Yes.	Yes.	.....	Died 5 days later.
38 Gentil, F. 27 33 53 68 5 hrs. 1902	.....	.....	.....	R. A.; 1 cm.; sutured.	....	....	.....	Recovered.
39 Gentil, F. 27 33 53 68 1904	.....	.....	.....	.....	....	....	Pericarditis; syphilis.	Died 17 hours later.
40 Gerzen 37 1902	Chloro.	Stab in fifth left space.	Resection of 5th and 6th ribs.	R. V.; sutured.	No.	Yes.	Pericarditis. pleuritis, nephritis, hemorrhage.	Died 53 days later.
41 Gerzen 37 1902	Chloro.	Cut under left costal arch.	Resection of 5th, 6th, 8th and 9th cartilages.	R. V.; 2.5 cm.; 4 sutures.	Yes.	Not opened.	Pericarditis and pleuritis.	Died 23 days later.
42 Gibbon 77 1902	1/4 hr. Chloro.	Knife cut through fourth left cartilage.	Resection of 3rd cartilage.	R. V.; 1.5 cm.; 1 suture; not completed.	....	....	.....	Died on table.
43 Gibbon 77 1905	About 3 hrs. Ether.	Knife cut dividing fourth left cartilage.	Resection of 4th cartilage.	R. V.; 2 to 1/2 in.; 6 catgut sutures.	Yes.	Yes.	Pleura not wounded.	Recovered.
44 Giordano 40 1898	1/2 hr. None.	Knife cut in second left space.	Flap of 3rd and 4th ribs; hinge below space.	L. A.; 2 cm.; 4 silk sutures.	No.	Yes.	Left pleuritis. Right pulmonary abscess.	Died 18 days later.
45 Giordano 40 1902	.....	Knife cut in sixth left space.	Flap of 4th and 5th ribs; hinge internal.	L. V.; 2 cm.; 2 silk sutures.	No.	Yes.	.....	Died 1 1/2 hours later.
46 Giordano 40 1902	.....	Knife cuts in 3rd, 4th and 5th left spaces near nipple.	Flap of 4th and 5th ribs; hinge external.	L. V.; 2 cm.; 2 silk sutures.	No.	Yes.	Autoplastic operation required to close the opening.	Recovered.
47 Giudice 62 1905	Soon.	Knife cut in third left space.	Resection of 4th and 5th cartilages.	R. V.; 1 cm.; catgut suture.	Yes.	Yes.	Hemorrhage.	Died next day.
48 Giuliano 41 1903	.....	Stab of third left space in nipple line.	Flap of 3rd and 4th ribs; hinge external.	L. A.; sutured with silk.	Yes.	Yes.	.....	Recovered.
49 Goebel 27 1905	1 hr.	Pistol ball, 7 mm.	Flap of ribs; hinge external.	L. V.; entrance and exit; both sutured with catgut.	Yes.	Yes.	None.	Recovered.
50 Grekow and Zeidler 26 37 1903	3 hrs. Chloro.	Knife cut in second left space, 5 cm. from sternum.	Resection of 3rd and 4th ribs.	L. V.; 0.5 cm.; silk sutures.	No.	No.	None.	Recovered.
51 Grekow and Zeidler 26 37 1903	5 hrs. Chloro.	Knife cut outside left nipple.	Resection of 3rd, 4th and 5th ribs.	R. V.; near apex; 1.5 cm.; 2 silk sutures.	No.	Yes.	Pericarditis and pleuritis.	Died 60 hours later.
52 Grekow and Zeidler 26 37 1903	4 1/2 hrs. Chloro.	Knife cut in second left space.	Resection of 3rd to 6th ribs.	R. V.; 1.25 cm.; 5 silk sutures.	No.	No.	Pericarditis and pleuritis.	Died 13 days later.

53	Guenot 20 25 1904	1½ hrs. Ether.	Knife cut in fourth left Flap of 3rd, 4th, 5th L. V.; near apex; 1.5 hinge internal.	No.	Yes.	Pleuritis.	Died 53 hours later.
54	Guenot 20 25 1905	1 hr. Chloro.	Knife cut in second Flap of right 3rd, 4th, R. V.; 1 cm.; 3 catgut from sternum. 2 cm. 5th and 6th ribs; sutures.	No.	No.	Hemorrhage in right Died 28 hours later.	
55	Guinard 18 1904	1½ hrs. Chloro.	Ponlard stab in fourth Flap of 3rd, 4th, 5th L. V.; interrupted catgut line. hinge external.	No.	Yes.	.....	Died 18 hours later, from aneurism.
56	Harte 3 1906	Ether.	Knife cut in third left Resection of 4th and 5th L. A.; ½ inch; interrupted catgut sutures.	No.	Yes.	Pleurisy and double Died 16 hours later.	
57	Henrikson 37 1906	.....	Stab in third left space. Resection of 3rd and 4th L. V.; 1.5 cm.; sutures.	....	....	.....	Died 16 hours later.
58	Hesse 26 27 72 1905	About 1 hr. Chloro.	Scissors wounds in left Flap of 3rd and 4th ribs; R. V.; near apex; 3 catgut sutures.	Yes.	Yes.	Pericarditis and pleu- Recovered.	
59	Hesse 26 27 72 1905	1½ hrs. Chloro.	Knife cut in fourth left Flap of 3rd and 4th ribs; L. V.; 0.5 to 0.75 cm.; space near sternum.	Yes.	Yes.	Pericarditis and pleu- Recovered.	
60	Hill 53 57 58 1902	8 hrs. Chloro.	Knife cut in fifth left Flap of 3rd, 4th and L. V.; ¼ inch; 1 catgut line. space within nipple; 5th ribs; hinge internal.	No.	Yes.	..... Recovered.	
61	Horodvinski 1899	None.	Knife cut in third left Resection of 3rd, 4th R. V.; 1.5 cm.; 3 deep space, 2 cm. from sternum and 5th cartilages.	Yes.	Yes.	Pericarditis and pleu- Died 3 days later.	
62	Isanardi and Columbino 27 29 1902	At once. Chloro.	Knife cut in sternum at Resection of 5 ribs. R. V.; 1.5 cm.; 3 sutures.	....	Yes.	Pleuritis.	Recovered.
63	Janari 1903	About 1 hr. Chloro.	Knife cut in third left Flap of 3rd, 4th and L. V.; 1 cm.; sutured.	Yes.	Yes.	Pleuritis.	Died 3 days later.
64	Kappeler 1904	2½ hrs. Ether.	Knife cuts over third rib Flap of 3rd and 4th L. A.; 1 cm.; sutured. and in third left space. ribs; hinge internal.	....	Yes.	Pleuritis. Jet of red blood with each diastole.	Recovered.
65	Kosiński 1899	.....	Knife wound in third left space.	....	....	..... Recovered.	
66	Lastaria 1901	½ hr. Chloro.	Knife cut in fifth left Flap of 3rd, 4th, 5th R. V.; silk sutures.	....	Yes.	..... Died next day.	
67	Launay 10 13 1902	4 hrs. Chloro.	Pistol ball 7 mm.; in Flap of 4th, 5th and L. V.; perforated; entrance and exit closed.	Yes.	Yes.	..... Recovered.	
68	Lemaître 14 76 1903	1½ hrs. Chloro.	Knife cut in fourth left Flap of 3rd, 4th and L. V.; 4 cm.; 5 interrupted space; 25 small cuts 5th ribs; hinge ruptured catgut sutures.	No.	Yes.	Pleura filled with blood.	Died 24 hours later.
69	Lemaître 14 1904	About 1 hr. Chloro.	Ponlard stab in fifth left Flap of 3rd, 4th and R. V.; 3 catgut sutures.	No.	Yes.	Pleuritis.	Died 10 days later.
70	Lenormant 23 42 64 1905	7 hrs. Chloro.	Pistol ball in fifth left Flap of 4th, 5th and R. V.; 15 mm.; 3 silk sutures. Liver, stomach and bowels wounded.	Yes.	....	Syncope on table; traction on tongue and heart massage revived him.	Died 4½ hours later.
71	Lisanti 1899	Very soon. Chloro.	Knife wound in fourth Flap of 4th and 5th R. V.; silk sutures.	No.	....	Signs of cardiac aneurism at end of 2 months.	Recovered.
72	Liscia 37 1901	None.	Stab in fourth left space. Flap of 2nd, 3rd, 4th R. V.; 3 sutures.	....	....	Pericarditis and ne- pthritis.	Died 42 hours later.
73	Longo 1899	¾ hr. None.	Knife cut in fifth left Flap of 4th and 5th L. V.; 3 interrupted space 1 cm. outside nipple; hinge above.	....	....	.....	Died 15 minutes later.

No. Operator and Year of Operation.	Time between Wounding and Operation.	Location of External Wound and Instrument by which Inflicted.	Method of Exposing the Heart.	Cavity Wounded and Treatment.	Drainage of		Complications.	Result.
					Pericardium.	Pleura.		
74 Mallzewski 1889	None.	Knife cut in fifth left space in nipple line.	Resection of 5th and 6th ribs.	L. V.; apex; 3 silk sutures.	No.	Yes.	.....	Died 26 hours later.
75 Mallzewski 1889	None.	Knife cut in fourth left space without nipple line.	Resection of 3rd rib.	L. V.; 1.5 cm.; 3 interrupted silk sutures.	Yes.	Yes.	Pericarditis and pleuritis.	Died 3 days later.
76 Mantouffell 26 1903	9 hrs. Ether.	Pistol ball, 5 mm. in fourth left space.	Resection of 4th, 5th, 6th and 7th cartilages.	R. V.; went through anterior wall and lodged in posterior, where it could be felt. Incision and removal. Silk sutures closed both wounds.	No.	Yes.	Pericarditis; aspirated.	Recovered.
77 Marlon 1898	2 hrs. Ether.	Pistol ball, fourth left space, 3 cm. from sternum.	Resection of 6th and 7th cartilages and part of sternum.	R. V.; perforated. Anterior wound sutured.	....	....	Ball did not open pericardium.	Died on table.
78 Maseill 1900	1½ hrs.	Knife cut 1 cm. within and below left nipple.	Resection of 6th rib.	L. V.; near apex; several sutures.	No.	Yes.	.....	Died 12 hours later.
79 Maucisire 37 1903	None.	Wound of left breast 8 cm. from sternum.	Flap of 3rd and 4th ribs.	Heart wound; 3 sutures.	Yes.	Yes.	.....	Died 24 hours later.
80 Mignon and Steur 1901	1 hr.	Knife cut in fourth left space 2 finger breadths from nipple.	Resection of 4th, 5th and 6th cartilages.	R. V.; 1 cm.; silk sutures.	Yes.	Yes.	.....	Died 2 hours later.
81 Miled 45 1902	About 2 hrs. Chloro.	Knife wound in fifth left space.	Resection of 6th rib.	R. V.; 15 mm.; 1 deep and 3 superficial silk sutures.	Yes.	Yes.	Anemia.	Died 15 hours later.
82 Miled 1903	About 1 hr. Chloro.	Knife cut in fourth left space near sternum.	Resection of 4th cartilage.	R. V.; 1 cm.; 1 deep and 2 superficial silk sutures.	No.	Yes.	Pericarditis.	Died 7 days later.
83 Morestin 9 1903	21 hrs. Chloro.	Pistol ball, 8 mm. caliber, in sternum opposite fourth cartilage.	Cut through sternum.	R. V.; 1 opening; 4 catgut sutures.	Yes.	Yes.	Ball is found in cavity of R. V.	Died 19 hours later from embolism.
84 Musummed 30 1905	Soon. Ether and Chloro.	Knife cuts in fourth and fifth left spaces.	Flap; hinge internal.	R. V.; sutured; suture of 3 intestinal wounds also.	No.	....	.....	Died 18 hours later.
85 Nauu 1900	.....	Knife cut in third left space, 4 cm. from sternum.	Resection of 2nd, 3rd and 4th cartilages.	R. V.; 2 cm.; 2 interrupted sutures.	No.	Yes.	Pericarditis and pleurisy.	Died 4 days later.
86 Neumann 26 1905	.....	Stab below left costal arch.	Resection of 7th to 4th cartilages.	R. V.; sutured with pericardium.	....	....	Hemorrhage.	Died ¼ hour later.
87 Nicolai 1899	1½ hrs.	Knife cut in fourth left space midway of sternum and nipple.	Resection of 4th and 5th cartilages.	R. V.; near apex; sutured.	....	....	.....	Died 12 hours later.
88 Nietert 1901	2 hrs. None.	Knife cut in fifth right space at sternum.	Resection of 5th and 6th cartilages. Pleura not opened.	R. V.; ½-inch; 3 interrupted silk sutures.	....	....	Anuria; death from shock and pericarditis.	Died 33 hours later.
89 Nietert 1901	More than 40 hrs. Chloro.	Knife cut in sixth left space within nipple line.	Flap of 5th and 6th ribs; hinge internal.	L. V.; ¾-inch; 2 sutures; may not have penetrated.	Yes.	Yes.	Pleurisy.	Recovered.

90 Nimier 5 27 1906	25 mins. Chloro.	Knife cut in fourth left Flap of 4th, 5th and R. V.; 1 cm.; 4 catgut sutures; hinge opened; pleura not num.	Yes.	.....	.....	Died next day.
91 Ninni 1898	At once.	Knife cut in fifth left Flap of 4th and 5th L. V.; admitting finger; ribs; hinge internal. 3 sutures.	Yes.	.....	.....	Died on table.
92 Ninni 1901	1½ hrs.	space midway of ster- 5th cartilages and part num and nipple.	Yes.	Pericarditis and pleurisy.	.....	Died 3 days later.
93 Noll 1903	1½ hrs.	Pistol ball, 7 mm. in ..... L. V.; wound sutured.	Yes.	Pleurisy.	.....	Recovered.
94 Pagenstecher 1899	16 hrs.	Knife cut below and Resection of 5th car- L. V.; 3.5 cm.; 3 deep sutures; 1 superficial.	No.	Pleurisy.	.....	Recovered.
95 Pagenstecher 1901	2½ hrs.	Knife cut in fourth left Flap of 4th and 5th Left coronary artery space, 1 cm. from ster- cartilages; hinge in- divided; both ends secured with sutures.	Yes.	Pericarditis and pleu- ritis.	.....	Died 4 days later.
96 Parlevcechio 1898	8 hrs.	Knife cut in fifth left Resection of 5th rib. L. V.; apex; 3.5 cm.; 4 sutures.	No.	.....	.....	Recovered.
97 Parozzani 1897	5 hrs.	space. Knife cut in seventh left Flap of 5th, 6th, 7th L. V.; near apex; 2 space in nipple line. and 8th cartilages; cm.; 4 silk sutures.	No.	None.	.....	Recovered.
98 Parozzani 1897	1½ hrs. None.	Knife cut in third left Flap of 4th, 5th and L. V.; 15 mm.; 2 su- space; nipple line. 6th ribs; hinge in- tures.	No.	Necropsy. Wound of interventricular wall.	.....	Died 48 hours later.
99 Pecori 44 1903	.....	Knife. cut in fifth left Flap of 5th and 6th R. V.; sutured; first tore line. space within nipple ribs. out; others placed farther from margin.	Yes.	Hemorrhage.	.....	Died on table.
100 Picone 31 1904	Very soon.	Knife cut two finger Flap of 3rd, 4th and L. V.; sutured.	Yes.	Hemorrhage in right pleura.	.....	Died 2 days later.
101 Pomara 1902	None.	Knife cut in sixth left Resection of 5th and L. V.; near apex; silk space below nipple. 6th ribs.	No.	Pericarditis and pleu- ritis.	.....	Died 73 hours later.
102 Qurcu 23 1906	2½ hrs. Chloro.	Knife cut in third left Flap of 3rd, 4th and L. V.; 2 interrupted space. 5th ribs; hinge ex- sutures.	No.	Syncope on table. Re- traction on tongue revived him.	.....	Recovered.
103 Ramoni 1899	1½ hr. Chloro.	Ponard stab over fifth Flap of 4th and 5th ribs; R. V.; 2 wounds; 4 left cartilage. 2 cm. hinge below.	Yes.	.....	.....	Recovered.
104 Rehn 8 1896	More than 24 hrs. Chloro.	Knife cut in fourth left Resection of 5th car- R. V.; 15 mm.; silk space. 2 cm. from ster- tialage.	Yes.	Pleuritis.	.....	Recovered.
105 Rehn 8 1906	8½ hrs. Chloro.	Knife cut in fourth left Flap of 4th and 5th R. V.; 10 silk sutures.	No.	.....	.....	Died 2 days later.
106 Renou 70 1902	Chloro.	Knife cut in fourth left Resection of 4th and L. V.; apex; 4 inter- space 4 cm. within 5th ribs.	.....	.....	.....	Died next day.
107 Ribas y Ribas 66 1906	About 1 hr.	nipple line. Stab in third left space. Flap of 4th, 5th and L. V.; 1 cm.; 3 su- 3 cm. from sternum. 6th ribs; hinge ex- tures.	Yes.	.....	.....	Died 72 hours later.
108 Riche 15 19 24 26 1902	2 hrs. Chloro.	Knife cut in fourth left Flap of 3rd, 4th and R. V.; 5 mm.; sutured.	No.	None.	.....	Recovered.
109 Riche 15 19 24 26 1904	1½ hrs. Chloro.	line and nipple. Pistol ball, 8 mm. in Flap of 3rd, 4th and L. V.; 2 wounds; cat- fifth left space, within 5th ribs; hinge ex, gut sutures in both.	.....	.....	.....	Died on table.
110 Rosa 1899	At once. None.	and below nipple. Knife cut in fifth left Resection of 5th, flap L. V.; base; 1.5 cm.; space. Resection of 6th, 7th and 8th; hinge below.	Yes.	.....	.....	Recovered.



No. Operator and Year of Operation.	Time between Wounding and Operation. Anesthetic.	Location of External Wound and Instrument by which Inflicted.	Method of Exposing the Heart.	Cavity Treatment.	Drainage of		Complications.	Result.
					Pericardium.	Pleura.		
111 Rothfuchs 26 1905	.....	Bullet.	Resection of 4th and 5th ribs.	L. V.: perforated; cat-gut suture in both wounds.	....	Yes.	Ball went through stomach and lodged in diaphragm.	Died 24 hours later. Peritonitis.
112 Savariaud 23 1902	Chloro.	Knife cut in fifth left cartilage 3 cm. from sternum.	Flap of 4th ribs; hinge external, not opening pleura.	5th R. V.: near apex; 3 sutures.	Yes.	Yes.	Gangrene of border of lung.	Died 52 hours later.
113 Savariaud 23 1904	Chloro.	Knife cut below and within left nipple.	Flap of 3rd, 4th and 5th ribs; hinge external.	R. V.: 3 catgut sutures.	No.	No.	Pericarditis and pleuritis.	Died 14 days later.
114 Schachowski 37 1903	.....	Knife cut in sixth left space, near nipple line.	Resection of 5th and 6th cartilages.	R. V.: 1.5 cm.; 6 sutures.	Yes.	....	.....	Recovered.
115 Schubert 26 1904	1/2 hr. Chloro.	Bullet in fourth left space.	Resection of 4th rib.	Two wounds in heart; 1 anterior. 1 posterior, both sutured with catgut.	....	....	Operator thought ball went through interventricular septum without opening a ventricle.	Recovered.
116 Schwerin 1903	3/4 hr.	Sharp-pointed body entered fourth left space.	Resection of 4th and 5th cartilages.	R. A.: 3 silk sutures.	Yes.	Yes.	Pericarditis, pleurisy and pneumonia.	Recovered.
117 Seini 37 1904	Chloro.	Stab in sixth left space in nipple line.	Flap of sternum and 4th, 5th and 6th cartilages.	L. V.: 3 cm.; 6 sutures.	No.	Yes.	.....	Died 3 days later.
118 Smith 74 1904	1/2 hr. Ether.	Knife cut in fourth left space, 2 cm. from sternum.	Resection of 4th and 5th ribs and part of sternum.	R. V.: continued silk sutures.	No.	Yes.	Pericarditis.	Died 7 days later.
119 Soave 69 1907	Very soon. Chloro.	Knife cut in fifth left space, 4 finger breadths from sternum.	Flap of 4th and 5th ribs; hinge internal.	R. V.: silk sutures.	Yes.	Yes.	None.	Recovered.
120 Somerville 47 1904	55 mins. Ether.	Knife cuts in fourth and fifth spaces within nipple line.	Flap and operation through 4th space; interrupted silk sutures.	L. V.: ragged 3/4 in.; 3 sutures.	Yes.	Yes.	None.	Recovered.
121 Stewart, F. 1 1902	At once. Ether.	Knife cut in fourth left space, 1 1/2 in. from sternum.	.....	L. V.: 3/4-inch; 6 catgut sutures.	....	....	.....	Died 2 days later.
122 Stewart 1904	3/4 hr. Ether.	Knife cut in second left space, 1 inch from sternum.	Flap of 3rd and 4th ribs; hinge internal.	L. V.: 3/4-inch; 6 continuous silk sutures.	Yes.	Yes.	Pneumonia and wound infection.	Recovered.
123 Stewart, G. D. 1902	1 1/2 hrs. Chloro.	Knife cut in 5th space, 1/2 in. in left nipple line.	Fifth rib resected.	L. V.: 3/4 in. sutured; 6 stitches.	Yes.	Yes.	Pericarditis and pleuritis.	Died 2 1/2 days later.
124 Steyer 37 1903	Chloro.	Stab about fifth rib near sternum.	Resection of 4th and 5th ribs.	R. V.: 4 sutures.	Yes.	Yes.	.....	Recovered.
125 Stude 1904	About 2 hrs.	Knife cut in chest.	Flap of sternum and 4th and 5th cartilages; hinge on right.	L. V.: 2.5 cm.; sutured.	....	....	Death due to pneumonia.	Died on table.
126 Sultan, C. 11 27 1905	.....	Two stabs in fifth left space, 2 cm. within nipple line.	Flap of 5th, 6th and 7th ribs; hinge external.	L. V.: 7 mm.; 4 sutures.	No.	No.	Necropsy: one liter of blood in pleura. R. V. found wounded.	Died 48 hours later.

		5 days.	Knife cut in second left Flap of 3rd, 4th and L. V.: silk sutures space, a finger breadth 5th ribs; hinge in- within nipple.	Yes.	Yes.	None.	Recovered.
127 Sultan, C. 11 27 1906							
128 Sultan, G. 24 1907		30 hrs. Chloro.	Pistol ball, 9 mm.; in Flap of sternum and L. V. cavity not fifth left space inside left 4th and 5th cartilages; hinge on right nipple line.	....	Not op- ened.	None.	Recovered.
129 Thiemann 7 1906		About 4 hrs. Chloro.	Needle in 4th left space. 5th ribs; needle fixed 1.5 cm. first closed at lower border of 4th rib.	Yes.	Yes.	Pericarditis.	Recovered.
130 Travers 49 1906		About 3 hrs. Chloro.	Iron picket wound Flap of 3rd, 4th and R. V.: 2 1/2 inches; 23 through lower end of 5th left cartilages and sutures; 3 fragments of sternum; hinge below.	Yes.	Yes.	Death due to clot in pericardium.	Died 10 days later.
131 Tscherniachowski 27 30 48 1904		Less than 1 hr. Chloro.	1 Knife cut in fourth left Resection of 4th car- L. V.: 1.5 cm.; 3 silk space, internal to nipple tilage.	Yes.	Yes.	None.	Recovered.
132 Tuzzi 1899		None.	Knife cuts in fourth left Resection of 4th and L. V.: 2 wounds; 1 space near sternum. 5th ribs.	No.	Yes.	Pericarditis and pleu- ritis.	Died 21 days later.
133 Vaughan 54 1901		Less than 1 hr. Ether.	1 Knife cut dividing fifth Flap of 4th and 5th car- L. V.: 2.5 cm.; 1 con- tilage hinge above.	....	....	....	Died on table.
134 Vaughan 54 1903		About 1 hr. Ether.	Knife cut in fourth left Flap of 4th, 5th and R. V.: 1 1/2-inch; 12 con- space near nipple. 6th cartilages; hinge internal.	No.	No.	Delirium tremens.	Recovered.
135 Velo 1902		About 1 1/2 hr.	Knife cut in sixth left Resection of 5th and L. V.: apex; 15 mm.; space in nipple line. 6th ribs.	Yes.	Yes.	Pleuritis.	Died 3 days later.
136 Vince 46 1903		About 12 hrs. Chloro	Ponlard stab in fifth left Flap of 5th, 6th and L. V.: 3 silk sutures.	No.	....	....	Died next day.
137 Vogel 1903		About 12 hrs. Chloro.	Wound in fourth left Resection of 4th and R. V.: 1.5 cm.; 5 silk space near sternum. 5th cartilages.	No.	Yes.	Pericardium opened and drained on second day. Su- tures in heart were finally ex- pelled.	Recovered.
138 Walker 1900		None.	Knife cut below left Abdomen opened, re- R. V.: sutured; tore costal arch. section of 6th and 7th out.	....	....	Diaphragm wounded.	Died 3/4 hour later.
139 Walker 1901		4 hrs.	Knife cuts 20, in heart Resection of 4th rib. 8 wounds of heart; L. V. penetrated twice; in fourth left space.	Yes.	Yes.	....	Died 1 1/2 days later.
140 Watten 1900		6 hrs. Chloro.	Knife cut in fourth right Flap of 3rd and 4th R. V.: 2 cm.; 3 sutures. ribs on right; hinge external.	Yes.	Yes.	....	Recovered.
141 Watts 1908		1 1/2 hr. Ether.	Knife cut in second left Resection of 2nd and R. V.: root of pulmo- space near sternum. 3rd ribs.	No.	Yes.	Blood in pericar- dium.	Died 1 month later.
142 Weinlechner 1904		Very soon. Chloro.	Knife cuts in third and Resection of 5th rib. L. V.: 5 mm.; silk su- fourth left spaces.	Yes.	Yes.	Pericarditis and pleu- ritis.	Died 49 hours later.
143 Weiss 67 1904 (?)		5 hrs.	Ponlard stab in heart Resection of ribs and R. V.: sutured. region.	....	Yes.	Pleuritis.	Died 15 days later.
144 Wendel 6 27 1905		About 5 hrs. Chloro.	Knife cut in fourth left Flap of 4th and 5th L. V.: 1 catgut suture, space, near sternum. cartilages; hinge ex- ternal.	Yes.	Not op- erated.	Pericarditis.	Recovered.

No. Operator and Year of Operation.	Time between Wounding and Operation.	Location of External Wound and Instrument by which Inflicted.	Method of Exposing the Heart.	Cavity Wounded and Treatment.	Drainage of		Complications.	Result.
					Peri-cardium.	Pleura.		
145 Wennerstrom 1906	2 hrs.	Fragment of glass in third left space near sternum.	Resection of 4th, 5th and 6th cartilages.	L. V.: 2 cm.; 1 catgut and 4 silk sutures.	No.	Yes.	3 gauze sponges left Recovered. in pleura; removed on 14th day.	
146 Wilms 27	2 hrs.	Pistol ball, 6 mm.	Inter-costa. Incision.	L. V.: perforated; both sutured.	No.	No.	None.	Recovered.
147 Wolff 35	.....	Knife cut.	.....	R. V.: 2 cm.; sutured.	No.	No.	Pericarditis and pleu-ritis.	Died 14 days later.
148 Ziembiski 37	.....	Stab wound.	.....	Heart wound; sutured.	.....	.....	.....	Died.
149 Zulehner and Brenner 1901	24 hrs.	Knife cuts. 12.1 in left space, 1 opening abdomen.	Resection of 3th, 6th and 7th cartilages.	R. V.: 2 cm.; sutures tore out.	.....	.....	Myocardium very friable.	Died on table.
150 Zulehner and Brenner 1901	.....	.....	.....	R. V.: 1 cm.; catgut sutures.	.....	.....	.....	Recovered.

## BIBLIOGRAPHY.

1. Am. Jour. Med. Sc. September, 1904 (Stewart). 2. Am. Med. Philadelphia, 1904, viii, 448 (Holladay). 3. Ann. Surg., February, 1885 (Dalton). 4. 1885, p. 209 (Harten). 5. Arch. f. klin. Chir., 1906, lxxx, 214 (Wendell). 7. *ibid.*, 1907, lxxiii, 565 (Thiemann). 8. *ibid.*, 1907, lxxiii, 723 (Rehn). 9. Arch. gen. de med., 1903, li, 2389 (Morestin). 10. *ibid.*, 1904, li, 2869 (Launay). 11. Brit. z. klin. Chir., Tubingen, 1906, l, 491 (Sultan, C.). 12. Brit. Med. Jour., 1903, i, 1285 (Dovle). 13. Bull. Acad. de med. Paris, 1902, 3 s., xvii, 141 (Launay). 14. Bull. Soc. anat. de Paris, 1903, lxxviii, 515 (Lemaitre). 15. *ibid.*, 1904, lxxix, 370 (Riche). 16. *ibid.*, 1905, p. 835 (Bréard and Morel). 17. *ibid.*, 1906, lxxxi, 318 (de Fourmestraum). 18. Bull. Soc. de Chir. de Paris, 1904, n. s., xxx, 705 (Guinard). 19. *ibid.*, 1906, new series, xxxi, 172 (Riche). 20. *ibid.*, 1906, new series, xxxi, 325 (Guenot and Desmarest). 21. *ibid.*, 1905, new series, xxxi, 818 (de Fourmestraum). 22. *ibid.*, 1905, new series, xxxi, 822 (Picquet). 23. *ibid.*, Paris, 1903, new series, xxxi, 142 (Gaudemet, Quénu, Savariand, Camus, and Lenormant). 24. *ibid.*, Paris, 1907, lxxviii, 142 (Baudet, Duval, and Riche). 25. Bull. méd., Paris, 1904, xviii, 585 (Guénot). 26. Centr. bl. f. Chir., 1906 (Schubert, von Manteuffel, Hesse, Neumann, Grekow, Riche, and Rothfuchs). 27. *ibid.*, 1906 (Bréard and Morel, Borchard, Dolcetti, de Fourmestraum, Gentil, Goebell, Isnard, Hesse, Nimier, Sultan, C. Tscherniackowski, Wendel, and Williams). 28. Centr. bl. f. d. Grenzgeb. d. Med. u. Chir., June 17, 1906, xi, No. 11 (Venus). 29. Clin. chir. Milan, 1903, xi, 381 (Piccone). 30. *ibid.*, 1906, xlii, 641 (Musumeci). 31. *ibid.*, Milan, 1929 (Piccone). 32. *ibid.*, 1905, 103 (Carmelo). 33. Cong. internat. de méd., Lisbon, 1906, Sec. ix, 446 (Gentil). 34. Deutsch. med. Wchnschr., Feb. 13, 1908 (Sultan, G.). 35. Deutsch. Ztschr. f. Chir., Leipzig, 1903, lxx, 67 (Wolff). 36. *ibid.*, 1906, 288 (Tscherniackowski). 37. *ibid.*, (Baliya, Durante, Liscia, Henriksen, Gerzen, Grekow-Zeidler, Maulclair, Steyner, Schachowski, Senai, Bardenheuer, and Ziembiski). 38. Edinb. Med. Jour., 1904, n. s., xv, 451 (Cummings and Beattie). 39. Gazzetta Clinica, S. Paulo, 1906, iii,

- 386 (Alves de Lima). 40. Gazz. d. osp., Milan, 1903, xxiv, 49 (Giordano). 41. Gazz. d. osp. e d. clin., 1905, 322 (Giuliano). 42. Gazz. d. osp., Paris, 1906, lxxix, 1239 (Lenormant). 43. Gazz. d. Acad. di Farino, 1903, ix, 263 (Colombini). 44. Pottolico, Rome, 1902-1903, 501 (Pecore). 45. *ibid.*, 1904, 1287 (Milesi). 46. Jour. de chir. et Ann. Soc. belge de chir., 1903-4, lii, 198 (Vince). 47. Lancet, London, 1904, 1278 (Somerville). 48. *ibid.*, 1905, li, 1482 (Tscherniackowski). 49. *ibid.*, 1906, li, 706 (Travers). 50. *ibid.*, 1906, li, 815 (Fischer). 51. Leo, G.: Contribution des plaies du cœur, 80 Paris, 1904, 52. Marseille méd., 1905, xlii, 54 (Dutour). 53. Méd. contemp., Lisbon, 1906, series 2, viii, 100 (Gentil). 54. Med. News, New York, December, 1901 (Vaughan). 55. München. med. Wchnschr., 1897, March 27, 437 (Williams). 56. *ibid.*, 1900, December (Hill). 57. *ibid.*, 1901, lix, 870 (Hill). 58. *ibid.*, 1902, November (Hill). 59. München. med. Wchnschr., 1904, li, 16 (Ritter). 60. Medycyna, Warsaw, 1904, xxxii, 506 (Borymowski). 61. Montreal Med. Jour., 1906, xxxv, 539. 62. Pammato, Geno, 1905, ix, 74 (Gudicelle). 63. Progr. méd., Torino, 1904, lii, 14 (Sartirana and Borsotti). 64. Progr. méd., 1907, series 3, xxxii, 854 (Lenormant). 65. Rev. de chir., Paris, 1905, xxxi (Gulbal). 66. Rev. de méd. y cirug., Barcelona, 1906, xx, i (Ribas y Ribas). 67. Rev. méd. de l'est, 1905, xxxvii, 504 (Weiss). 68. Rev. portug. de méd. e cirurg., Lisbon, 1901, x, 353 (Gentil). 69. Riforma med., Naples, 1908, xlix, 121 (Soave). 70. St. Louis Cour. Med., 1905, xxxii, 335 (Campbell). 71. Sitzungs. d. ärzt. ver., Nürnberg, 1906 (Zimmermann). 72. Sitzungs. d. physik. med. Gesellsch. zu Würzburg, 1905 and 1906 (Hesse). 73. Soc. Lanciana d. cap. di Roma, 1904, p. 239 (Capello-Cimoroni). 74. South. Cal. Fract., Los Angeles, 1904, xix, 337 (Smith). 75. Surgery of the Heart and Lungs (Ricketts). 76. Thèse de Paris, 1905 (Lemaitre). 77. Tr. Coll. Phys. Phil., 1905, series 3, xxvii, 213 (Gibbon). 78. *ibid.*, 1906, series 3, xxviii, 88 (Roberts). 79. Tribune méd., Paris, 1904, old series, xxxvi, 29 (Renon). 80. Ungar. med. Presse, 1907, xli, 19 (Fischer).

**RUPTURE OF THE HEART.**

The heart may rupture from overdistention of one of its chambers—most frequently, it is said, the left ventricle—from the bursting of an aneurism or abscess, from embolism of a coronary artery, from the spasm of tetanus, possibly from violent exertion, and from blows on, or compression of, the chest. While disease of the myocardium is often a predisposing cause, yet it is evident that rupture of a sound myocardium may occur.

Autopsy of a man who had fallen from a third-story scaffolding, striking a horizontal iron bar at a distance of six meters from the ground. Death had been instantaneous. The heart was normal in size, somewhat flabby, and showed an increase of fat. Two cm. from the apex of the anterior wall of the right ventricle a rupture of the muscular fibers was noted, opening into the cavity of the ventricle.

This case affords an example of indirect traumatism to the heart, which rarely gives rise to rupture of this organ. Alessi and Pieri (*Riforma Medica*, Nov. 10, 1906).

Case showing that extensive trauma to the heart may occur with little or no injury to the thorax. An Italian, aged 44 years, was engaged in digging in a sand bank. His fellow workmen, a short distance removed, heard him cry out, and on turning about, found that the bank had caved in and the patient was surrounded up to the waist by a large quantity of sand. He was unconscious, but apparently alive. When dug out, he was dead. The anatomic diagnosis included multiple ruptures of the heart. Kellert (*Jour. Labor. and Clin. Med.*, July, 1917).

The **symptoms** are precordial distress, restlessness, syncope, dyspnea, rapid pulse, muffled heart sounds, and, perhaps, enlarged area of cardiac

dullness. Death is caused by the accumulation of blood in the pericardium and may be almost instantaneous, or the patient may live ten or eleven days, as in reported cases.

**Treatment.**—Operation holds out almost the only hope. Perhaps a small minority in whom the rupture is very small may recover under the influence of quiet—in other words, may recover spontaneously. In spite of the opinion—by no means proved to be a fact—that rupture nearly always means a diseased heart muscle, no hesitation should be felt in treating the patient as if he had received a stab or gunshot wound of the heart. Even if the myocardium is diseased, it will probably hold stitches and the closed wound will heal, unless the exciting agent which produced the rupture is again permitted to act.

**SURGICAL DISEASES OF THE PLEURA AND LUNG.**

**PLEURITIC EFFUSIONS.**—This term is used to cover all cases in which a collection of fluid occurs in the pleural sac. The most frequent cause of this condition is inflammation of the pleura, or pleuritis, which passes the fibrinous or plastic stage and goes on to the condition of pleurisy with effusion. In such cases the character of the fluid in the chest may present any gradation from a straw-colored serum to a thick, creamy pus. In a smaller number of cases, all inflammatory conditions of the pleura may be excluded, and yet fluid be present because of renal or cardiac disease or both: hydrothorax, because of trauma: hemothorax, or because of disease or injury to the thoracic duct: chylothorax. The exudate in pleurisy with effusion may,

however, be more or less hemorrhagic in character and quite rarely chyloform. It will be necessary to consider here the surgical features of pleurisy with effusion with both sero-fibrinous and purulent exudates, hemothorax, and hydrothorax.

The predisposing factors to pleuritis are of slight moment. Trauma and exposure occasionally seem to be the starting point. The condition is more frequent in males. Like most respiratory diseases, it is more frequent during the months of winter and early spring. Infections are probably the exciting cause in all cases. The tuberculous nature of pleurisy in a considerable percentage of the cases is being recognized. The pneumococcus, the streptococcus, the staphylococcus, and, indeed, practically all the pyogenic organisms play a more or less important part in the etiology of pleurisy, either alone or as mixed infections.

#### **Pathology and Symptomatology.—**

The pathology of the pleura itself in pleurisy with effusion is that of any inflammatory condition of serous membrane. As far as the effusion is concerned, as has been said, every possible gradation is encountered. The fluid is frequently clear and straw colored. In other cases it is more or less deeply tinged with blood. Flakes and flocculi of fibrin are practically always present. The admixture of cellular elements increases the cloudiness, and no sharp lines of demarcation can be drawn between serous, seropurulent, and purulent exudates. The symptoms of pleurisy with effusion are those of the toxemia resulting from the infection, those due to the physical effect of the exudate on the mechan-

ics of respiration and circulation, and those elicited by examination of the patient, the physical signs.

The first two may be considered together. The onset is insidious in the majority of cases. In secondary pleurisy the symptoms may be so slight as to escape detection save by routine examination or necropsy. The typical symptoms of the onset in primary cases are chilliness, fever, pain in the side, and slight cough. The characteristic symptoms of acute infectious processes, malaise, anorexia, increased pulse rate, generalized pains, febrile urine, are usually present. When the accumulation of fluid is rapid, dyspnea and a rapid, feeble pulse are likely to be present. The course of the disease is variable in the extreme. The pain generally decreases with the accumulation of fluid, which prevents friction between the inflamed visceral and parietal pleuræ. In cases with a decidedly purulent exudate (empyema), the general symptoms are more distressing. The fever tends to be higher and has a septic character; chills, sweats, pallor, and rapid emaciation are likely to be present.

As to inspection, the patient generally prefers to lie on the affected side. The chest on the side of the effusion looks larger; the intercostal spaces may appear to be obliterated or may even bulge. The excursion of the chest during respiration is diminished on this side. The apex beat may be seen to be displaced. Palpation tends to confirm the findings of inspection. Except in the rarest cases tactile fremitus is absent over the effusion. Over the area of the effusion the note elicited on percussion is flat, almost entirely lacking in resonance, and in

addition the finger appreciates a sense of resistance. The height of the fluid as shown by percussion varies with the upright or reclining position of the patient.

Pitres's coin sign, first described in 1898, is obtained in the following manner: An assistant holds firmly against the thorax of the pleuritic subject about to be examined a small copper coin. He strikes this with a second coin, while the examiner applies his ear to the opposite side of the chest at the same level. Certain acoustic phenomena become noticeable. If the sound has to pass through spongy or alveolar tissue it becomes muffled, but if a collection of gas interposes it becomes intensified. If a solid mass or liquid effusion interposes, a distinct metallic clink is heard. The writer found the "signe du sou" a very valuable test for exudate in the pleural cavity, including the determination of its boundaries, and is superior in this respect to percussion and the vocal fremitus. Slatowerschownikow (*Deut. med. Woch.*, June 27, 1912).

The presence of air above the pleuritic effusion, determined by means of roentgenoscopy when the patient is examined erect and then with the trunk inclined at an angle of about forty-five degrees, is a valuable sign. As the trunk is thus bent over, a clear space is seen above the level of the fluid, while in the erect position there is nothing to show the presence of the spontaneous pneumothorax. It suddenly comes into view on the screen as the level of fluid shifts. Kraus (*Beitrage z. Klinik d. Tuberkulose*, Bd. xxi, Nu. 3, 1912).

The paravertebral triangular area of dullness in pleural effusions, the Korányi-Grocco sign, is of considerable value. According to Gordinier (*Albany Medical Annals*, April, 1909), to Professor Korányi, of Budapest, rather than to Grocco, of Florence, belongs the honor of first directing, in 1897, the profession's attention to this

diagnostic sign in pleural effusions, namely, a triangular area of dullness on the side opposite to the pleural effusion. Grocco, on the other hand, independently described it in March, 1902, as follows, as quoted by Gordinier: "A new physical sign which he had observed in pleural effusions, a paravertebral triangle of the side opposite that of the pleural effusion. When with a pleural effusion of sufficient size, one percusses from above downward, along the spinous processes of the vertebræ, with the patient in the sitting posture, there appears at the level of the fluid a dullness which, relative at first, becomes absolute as one passes downward in association with a progressively increasing sense of resistance. In like manner, by percussing downward on the healthy side along lines parallel to the spinous processes, there is noted, opposite the dullness in the median line, a paravertebral area of deficient resonance of triangular shape. One side of this dull area is represented by the line of the spinous processes; another, by the lower border of the area of thoracic resonance for a short distance, which varies in length from 2 to 3 or more cm.; the outer side is represented by a line which, starting from the base, rises obliquely, to unite at an acute angle with the median line at about the upper limit of dullness. In right-sided effusion, other things being equal, the paravertebral triangle has seemed to me more marked. Although symptomatology abounds in methods for differential diagnosis between pleural effusion and pulmonary infiltration, there can be no doubt that the sign which I have mentioned may be of value in some cases, espe-

cially in right-sided and encapsulated exudates."

The paravertebral triangular area of dullness was present in every one of the 27 cases of pleural effusion personally observed. It was absent in a case of left-sided encysted em-

shown by the autopsy, an exudate in the right pleural sac. The autopsy findings of a personal case proves, however, that the presence of a typical paravertebral triangular area of dullness may, as had been shown by Smithies and Ewart, be due to



Photograph from a case of left-sided pleural effusion showing Grocco's sign, relative dullness and absolute flatness, together with the triangular area of dullness of the opposite side. (Gordinier.) (Albany Medical Annals, April, 1909.)

pyema and present in a case of abscess of the right lobe of the liver which had displaced the diaphragm upward and so compressed the right lung that the whole right pleural cavity was effaced.

The physical signs in the case last mentioned were quite typically those of a right-sided pleural effusion, with a perfectly distinct paravertebral triangular area of dullness of the opposite side without, as

extrathoracic disease. It also showed that, while the Korányi-Grocco sign is of great diagnostic value in the recognition of pleural effusion, it is by no means pathognomonic. As the writer has found in massive pneumonias moreover, a dullness over the lower spine exists, producing an area of dullness parallel to the spine, but not of a triangular shape. H. C. Gordinier (Albany Med. Annals, April, 1909).

Paravertebral dullness, when decidedly triangular in shape, is fairly distinctive of pleural effusion when associated with signs of intrathoracic diseases. It also seems certain that it is of distinct value in the recognition of small effusions, and of encapsulated effusions, provided that these are in contact with the spinal column. When the triangle does occur as a result of disease below the diaphragm, it is usually symmetrical, differs in shape from the typical triangle of pleural effusion. Blumer (*Yale Med. Jour.*, Jan., 1909).

Grocco's paravertebral thoracic triangle of dullness, due to fluid free in the pleura, is rectilinear, not curved, and in other respects also agrees with the description of it given by Grocco. It is also produced by fluid collections in the abdomen; its base is then broader than in pleural cases. In the latter neither its width nor its shape vary appreciably, but only its height; this rises exactly to the level reached by the effusion itself. In bilateral cases of pleural effusion a Grocco triangle can be made out on both sides, in spite of the dullness due to the two effusions. As the effusions are seldom quite equal, two unequal Grocco's triangles are the rule. In ascites and analogous abdominal cases the rule is for the two triangles to be equal; they therefore make up together a low, but wide, equilateral triangle bisected by the spine. Ewart (*Lancet*, June 19, 1909).

Grocco's paravertebral triangle sign is found only in cases of pleural effusion, and is absent in pneumonia and pulmonary fibrosis, but it is not present in all cases of pleural effusion. The writer found it in 14 out of 19 cases only. This agrees with the earlier observations of others, but most clinicians now maintain its invariable presence in effusion. He has not observed any difference varying with the side on which the effusion existed, though some maintain that the dullness is best marked when the effusion is on the right side. The sign, when present, is of

great value; its absence is of less importance. Moorhead (*Dublin Jour. of Med. Sci.*, June, 1909).

In cases with free fluid in the pleural cavity, or in which an encapsulated effusion lies along the spine, the Grocco sign is practically constant. When the patient lies upon the affected side, diminution or disappearance of the triangle is noticed (except when the pleural cavity is enormously distended), reappearing when the patient assumes the sitting or standing position, or reclines on the other side. A more pronounced triangle is present in right-sided effusions. The hypotenuse of the triangle is usually a curved line, especially at the upper portion. The size of the triangle varies with the amount of pleural effusion, except that right-sided effusions usually present a somewhat larger triangle. The presence of this triangle is not pathognomonic; it may exist in subphrenic conditions accompanied by a fluid accumulation. Brown (*Lancet-Clinic*, June 15, 1912).

The auscultatory phenomena observed in cases of pleuritic effusion vary greatly, depending on the amount of the effusion and the condition of the lung as regards associated disease and the degree of its compression by the exudate. In early stages, even after some effusion has taken place, the pleuritic friction rub may be heard. With larger exudates the friction rub is usually absent. The breath sounds may be absent over the area of flatness or have a far-away, distant character. Bronchial breathing at the base of the lung is common. Inspiration is usually somewhat prolonged. Râles are frequently heard. With very large effusions the breath sounds may be practically entirely absent on the affected side.

Purulent effusions are far more common before the tenth year than they are afterward. Under 3 years



of age it is almost certain that the accumulated fluid is purulent. About 75 per cent. of empyemata in children are due to the pneumococcus. They may be divided into two groups—those associated with pneumonia and those which are primary; 17.6 per cent. of the empyemata of children are caused by the streptococcus. This infection may occur alone or be associated with the pneumococcus or the tubercle bacillus. The streptococcus is not infrequently found in empyemata secondary to suppurations in other parts of the body. About 25 per cent. of the empyemata in adults and children are due to the tubercle bacillus. It is rare to find the bacillus in purulent effusions. J. G. Emanuel (*Lancet*, Jan. 13, 1906).

Pleuritic exudates are rather common before the fifth year of life and rather more frequent in the right than on the left side. The symptoms are often acute in onset and liable to be taken for pneumonia, which frequently coexists. In the serous form the prognosis is generally good, and if there be no serious displacement or disturbance of respiration or circulation an expectant treatment may be all that is required; otherwise, aspiration is advisable. Empyema, however, seldom recovers without surgical treatment. The writer favors rib resection in these cases by means of J. D. Bryant's thoracotomy. M. Germann (*Jour. Amer. Med. Assoc.*, Oct. 20, 1906).

Pleurisy with effusion is a common affection in infants under 2 years of age. In the vast majority of cases it is purulent. Because of the disastrous and even fatal results of delay in, or mistakes of, diagnosis, it should be recognized early, so that prompt surgical treatment may be given. In arriving at a diagnosis, the antecedent affections should be fully appreciated. Of these, pneumonia is by far the commonest. The general symptoms, as well as the physical signs, should be carefully weighed. The latter are the more distinctive. The most reliable signs in the order

of their importance are (1) exploratory puncture; (2) dullness with a sense of resistance, and (3) displacement of the apex. The other signs, so valuable in differentiating effusions in the adult, are uncertain, variable, and confusing in infants. The recognition of localized collections of fluid is especially puzzling and demands great skill and a frequent resort to exploratory puncture or operation. The latter is safe, even when the lung is pierced, and particularly so when fluid is present. In view of the distressing results of unrecognized empyemas, it is imperatively demanded in all doubtful cases. The variability of the physical signs is a striking feature in infants and should always suggest an effusion. D. J. M. Miller (*Arch. of Ped.*, Jan., 1911).

Valuable signs of pleural effusions are elicited by examination of the heart. This is frequently displaced, in the great majority of cases, toward the sound side. In chronic pleurisy and after the formation of firm pleuropericardial adhesions the direction of displacement is reversed, *i.e.*, toward the affected side. Cardiac displacement is usually much more pronounced toward the right, *i.e.*, in left-sided pleurisies.

Personal cases suggest that right-sided pleural effusion tends to show that one cause of sudden death in cases of right-sided pleural effusion may well be occlusion of the great veins as they approach the heart, and more especially occlusion of the inferior vena cava. Geddes (*Brit. Med. Jour.*, Feb. 4, 1911).

**Diagnosis.**—The diagnosis of pleurisy with effusion should never be left in doubt, except in cases where it is evident that the exudate, if any exists, is very small and not purulent. The operation of thoracentesis is associated with so little danger in comparison with the danger of hesitation

and delay in cases of pleurisy with effusion that it should be undertaken much more frequently. The same may be said in regard to differentiation between purulent and serous exudates. The withdrawal of fluid by means of needle or trocar settles the question at once, constitutes the proper treatment for serous effusion, and permits the immediate exhibition of the proper procedures for empyema. Edema of the chest wall on the affected side and dilatation of the subcutaneous veins point toward purulent exudates, as do a disproportion between the apparent amount of the exudate and the severity of the general symptoms, or an undue cardiac displacement.

Having ascertained that there is fluid in the pleural cavity, its nature is to be determined. This is often possible by study of the temperature, by the presence of rigors and sweating, vocal resonance, bulging, and tenderness over the intercostal spaces, or by the history. An exploring needle should be used in doubtful cases. If pus is obtained and it is from the lung the microscope will reveal (a) catarrhal cells with carbonaceous pigment; (b) yellow, elastic lung tissue; (c) pus cells in rows separated by threads of mucus. In the examination of children it must be remembered (1) that there is no expectoration, and (2) that a child's voice does not give a tangible fremitus. If a diagnosis of pneumonia has been made, empyema should be suspected and an exploratory puncture made: 1. When there is undue delirium. 2. When there is marked oscillation of the temperature. 3. When there is tenderness over the affected side. 4. When there is fullness in one or more intercostal spaces in the area of dullness. 5. When there is prolongation of fever, with or without acute symptoms, beyond the period of pneumonia crisis.

6. When there is doubt as to the diagnosis, all possible precautions having been taken. Middleton (*Practitioner*, Nov., 1906).

Cholesterol crystals were numerous in the effusion in the right pleura of a man of 25 with minor signs of pulmonary tuberculosis. The pleurisy had a chronic tendency but, notwithstanding the persistence and recurrence of the effusion through 6 years, the general health kept good and the cholesterol crystals did not seem to cause many subjective symptoms. The crystals glistened in the effusion, as there was up to 0.41 per cent. cholesterol. The albumin content reached 5.23 per cent. The fluid was sterile. The effusion had developed after a spontaneous pneumothorax. P. Arnell (*Hygiea*, Aug. 16, 1917).

**Treatment.**—Any consideration of the medical treatment of pleurisy would be out of place here. One point may be emphasized, and that is the great frequency of tuberculosis as a cause or complication of pleurisy and the necessity of carefully watching cases after apparent recovery, and of instituting the proper hygiene. The surgical treatment will be found under the description of the operations involved, thoracentesis, thoracotomy, thoracoplasty, described farther on in this article and the medical treatment under Pleurisy. Among minor measures may be mentioned, in the present connection, however, the **insufflation of air**, **exposure to red or ruby light**, and the introduction of **superheated air**.

The writer discusses the value of the **insufflation of air** as a good method of evacuating a pleural effusion. This harmless method keeps up the compression of the lung, which prevents injury and promotes healing. The air takes the place of the heavy liquid and thus relieves the weight on the diaphragm. The

technique employed is simple: It consists of the insufflation of air with an ordinary bicycle pump or other vacuum pumps. This air is passed into a flask which has been used for aspiration and to receive the aspirated fluid. The insufflation should be arrested at the slightest discomfort on the part of the patient.

The writer reports a case in which he evacuated by this means 4.25 liters (4½ quarts) of effusion from a tuberculous process at one sitting. In other cases 4 and 4.8 liters (4¼ and 5 quarts) of effusion were removed by Drs. Dufour and Vaquez, respectively, at one sitting. Achard (*Semaine médicale*, Sept. 14, 1908).

The writer applied **superheated air** to one-half of the thorax in the effort to induce absorption of an effusion which had for months resisted all other measures. The heat was at first 80° and 100° C. (176° and 212° F.), increasing later to 120° and 140° (248° and 284° F.). The sittings were at first fifteen and later thirty minutes long, given every second day at first, then for two, three, and four days at a time. Prompt benefit followed; after 35 applications all signs of inflammation had vanished and the patient felt better than for years. Fellner (*Deut. med. Woch.*, April 15, 1909).

The early treatment of septic pleural effusions consecutive to chest wounds is advocated by the writers. The thorax then preserves its form and almost normal limits; radioscopy shows a normal permeability of the lung tissue. The recovery is thus more perfect. In chest wounds showing neither fracture nor effusion, the authors abstain from intervention. If there is a fractured rib or scapula they reduce the fracture and close. If there is a small foreign body, it is left; if the foreign body is of considerable size, it is extracted immediately if easily accessible. In other cases secondary extraction is preferred. If there is pleural effusion which cytological and bacteriological

examination shows to be septic, a low incision is made under local anesthesia on the posterior axillary line and some centimeters of the ninth rib resected. Foreign bodies in the affected area are extracted. The pleura is then disinfected by means of an intermittent irrigation of **Dakin's solution**. Fifteen cases were treated; there were 12 recoveries, 11 from pleural abscess, and 1 from subphrenic abscess. Combier and Hertz (*Bull. et mém. Soc. de chir. de Paris*, xliii, 1678, 1917).

A clinical and radioscopic study of 152 cases of traumatic and spontaneous disease of the pleura were followed, months and years afterward, by pronounced adhesions of the sheets of the pleura, over extensive areas, only in the cases of pleurisy of tuberculous origin. In all the other cases the adhesions were slight or transient as a rule, including the cases with simple hemothorax after a war wound.

Any extensive hemothorax persisting after several punctures is liable to produce symphysis between the layers of the pleura, as it undergoes organization. Péhu and Daguet (*Annales de Méd.*, Paris, July-Aug., 1917).

The writers advocate strongly the method introduced almost simultaneously by Depage and by Tuffier having for its purpose to sterilize the infected pleural cavity by the application of **Carrel's method**. As performed by Combier and Hertz, the procedure consists, first of all, in removing a section of the ninth rib 3 or 4 centimeters long, making a broad opening into the pleural cavity, and inserting two drainage tubes, the one short, with broad lateral openings near its tip to carry off fluids, and the second narrower and longer, inserted to an extent commensurate with the length of the thorax, that the apex of the lung may be reached by it if necessary. The 2 drains are fixed alongside in the wound and the opening into the pleura hermetically closed. From the shorter drain runs tubing into a ves-

sel half filled with Dakin's fluid. Dakin's fluid passes into the pleural cavity from above through the narrower tube and runs out again through the lower drain tube. Constantini and Vigot (*Paris méd.*, Jan. 26, 1918).

**HYDROTHORAX**, when extensive, may require the withdrawal of fluid on one or both sides by **thoracentesis**. Frequently, however, this condition yields to treatment directed toward the underlying renal and cardiac disease.

**HEMOTHORAX.**—The presence of more or less blood in cases of pleurisy with serous and purulent effusions has been noted. Its presence in pleuritic effusions of an inflammatory character has no bearing as an indication for or against surgical intervention. Cases of hemothorax of non-inflammatory origin are in the great majority of cases traumatic, although the rupture of aneurisms and the erosion of vessels by malignant growths of the lung or pleura are occasional causes. The traumatic cases are usually due to fracture of the ribs associated with splintering and bleeding from the torn lung. Stab and gunshot wounds act in an obvious way. Severe contusion of the chest wall may cause hemothorax without apparent injury to the ribs. In any case the source of the bleeding may be the intercostal vessels or vessels in the parietal pleura or the lung-tissue. The treatment of the traumatic cases, of course, involves the location of the bleeding point and its control by ligature or packing. These wounds will be considered under the head of wounds of the thorax.

In the campaign in Flanders hemorrhage appeared to be, and sepsis undoubtedly was, much more serious in

the prognosis of chest wounds than in the South African campaign. Death from simple hemorrhage is not to be feared if the patient survives to the third day. Of 328 cases of hemothorax seen during life, 211 were sterile, and 89 of these so large as to need aspiration; 117 were septic. Death occurred in 47, of which 36 were septic. Sterile hemothorax may disable a patient by prolonged fever, dyspnea, or progressive collapse of the chest wall. Absorption is slow. Hence free fluid should be removed whenever the effusion exceeds 20 or 30 ounces—that is, where the dullness reaches half-way up the scapula. The 7th to 10th day is convenient for **aspiration** provided fresh hemoptysis has ceased. A massive clot is uncommon. The needle should be introduced well forward in the axilla at the anterior limit of the effusion, and high up. If discomfort is noted, **oxygen** should be introduced. The gas is adequately sterilized by passage through a bacterial trap formed by 3 narrow loops on an open glass tube. Bradford and Elliott (*Brit. Jour. of Surg.*, Oct., 1915).

Open pneumothorax is treated by **mechanical cleansing and closure**. In infected hemothorax **resection of a rib** under combined **local and nitrous oxide and oxygen anesthesia, manual removal of the clot, washing the cavity and swabbing with an antiseptic**, and tight **closure** is the author's practice. Of 29 cases so treated, 16 remained closed, 13 were re-opened. After 48 hours the chest is aspirated. Foreign bodies the author believes should not be removed from the lung at the base hospital. Of the 450 cases, 127 caused by bullets, 50 by shrapnel and 272 by steel fragments, 27 died, 12 of septicemia, 6 of some form of pneumonia, with or without complications. Nineteen of the 27 were operated upon. W. Hutchinson (*Canad. Med. Assoc. Jour.*, viii, 972, 1918).

**GANGRENE AND ABSCESS OF THE LUNG.**—In properly selected

cases the attack of these conditions by surgical means is justifiable and often life-saving. The technique of the operations will be considered later.

Gangrene of the lung is the result of necrosis of a portion of lung-tissue, followed by its infection with ordinary putrefactive organisms. It is seen as a rare sequela of lobar pneumonia, and more commonly in cases of aspiration pneumonias and following the lodgment of foreign bodies in the bronchi. It may be a metastatic phenomenon following the lodgment of infested emboli in the lung-tissue, and a frequent cause is embolism or thrombosis of branches of the pulmonary arteries. Diabetes mellitus and all prolonged, debilitating diseases, as typhoid, may be considered as predisposing factors. It is an occasional sequela to abscess formation, and sometimes occurs around tuberculous and bronchiectatic cavities.

**Etiology.**—The etiology of pulmonary abscesses is in every way similar to that of gangrene. The cases are generally grouped into those abscesses occurring in previously infected lung-tissue, and those of a pyemic origin.

Abscess of the lung following operation on the tonsils and upper air tract was observed by the writer in 3 cases. One was operated upon and recovered. The other 2 made spontaneous recoveries. Embolism, infection of the lung, or aspiration of blood containing cheesy concretions or small pieces of tissue are possible causes. C. W. Richardson (*The Laryngoscope*, July, 1916).

The writer reports 3 cases of lung abscess in adults following tonsillectomy. A questionnaire sent to a number of laryngologists, internists

and surgeons tended to show that the majority of these cases occur after operation under general anesthesia, in young adults between 20 and 35. The lesions in most instances were aspiratory in origin, as evidenced by the location, the ease of aspiration, the occurrence of single abscesses in practically every case, the predominance of the complications, the free clinics and charity hospitals, and, finally, the number of analogous conditions that can cause lung abscess in no other way. A more general use of local anesthesia for tonsil surgery, the abolishment of rapid tissue destroying operations and a respectful attitude toward hemorrhage and the secretions of the operative field are recommended. Ira Frank (*The Laryngoscope*, June, 1917).

Gangrene of the lung is generally circumscribed, the necrotic area being walled off by a zone of active inflammatory reaction. Such foci may be multiple. Rarely the process is diffuse, especially following lobar pneumonia and the plugging of large arterial branches. In a large number of the cases the symptoms of abscess or gangrene of the lung are effectively marked by the symptoms of the primary disease, as lobar pneumonia or septicemia. The typical course in these cases is rapidly from bad to worse. Chills and high fever of a septic type are, of course, common. In the postpneumonic cases prolonged fever, or its return after the crisis with failure of resolution, is suspicious. The changes in the character of the sputum, however, are of the greatest diagnostic significance. This is usually greatly increased in amount and takes on an entirely different character. In cases of abscess a sudden, large expectoration of pus may occur following rupture of the abscess into a bronchiole. The puru-

lent expectoration has a bad odor, which is insignificant, however, in comparison with the sickening stench from the sputum and breath in cases of gangrene. The sputum in both cases usually contains elastic fibers and large amounts of detritus of pulmonary tissue. The presence of elastic fibers is of very considerable diagnostic import. The physical signs are rarely definite enough to be of great value. They are first those of consolidation followed by cavity formation.

**Treatment.**—In regard to the treatment of these conditions there can be no doubt that surgery offers the only hope. In fairly typical cases the diagnosis is usually little in doubt, the main difficulty coming in in locating the process. In this connection the physical signs of consolidation or cavity, or of involvement of the pleura, must all be taken into consideration. In many cases exact localization will be impossible and exploratory incision will have to be done. The object of surgical intervention is the removal of the gangrenous mass in one instance, the drainage of the abscess in the other.

Case of pulmonary abscess treated with **artificial pneumothorax**. The lung expanded again and the pleura resumed its normal position and function. The writer holds that when there is no tuberculosis of the pleura, or when this disease, formerly present, has gotten well, the long-continued separation of the pleura, or its contact with nitrogen, does not produce changes which interfere with its function, or cause its surface to adhere. Forlanini (Münch. med. Woch., Jan. 18, 1910).

Six cases in which **operative procedures** were done for abscess or gangrene of the lung. Recovery occurred in all but 1 case in which the

lesions were multiple and the patient a feeble child. The lung was entered from the rear in all the cases. Solieri (Deut. Zeit. f. Chir., Jan., 1911).

Case of abscess of the lung and liver in a child. The abscess was in the dome of the liver and had perforated through the diaphragm and lung into a bronchus. The involved organs were firmly bound together by adhesions. Drainage was very poor and was accomplished only through the process of expectoration and cough. The child had been ill for five years and nothing had given any relief. The writer adopted the plan of having the child lie on a table with his whole body dependent vertically, being supported by his legs only. While in this position he was made to strain and cough and was thus able to empty the cavity completely. This was repeated several times daily. The secretion became rapidly less, and in the short space of six weeks the abscess was healed and recovery was complete. McKechnie (Lancet, March 30, 1912).

The death-rate from acute pulmonary abscess upon medical or expectant treatment is 60 per cent.; upon surgical treatment, 30 per cent.; and, so far, under **artificial pneumothorax** treatment 10 per cent. C. W. Richardson (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 30, 1917).

The outcome is infinitely better in a gangrenous process in the lung when air is allowed to enter the chest. The lung retracts and the contents of the gangrenous focus are expelled in a vomica, after which recovery proceeds rapidly. **Artificial pneumothorax** should be applied early under screen control, and be completed and renewed a few days later. In a few cases he injected nitrogen, but usually air sufficed. Weill (Bull. de l'Acad. de Méd., Oct. 29, 1918).

**NEW GROWTHS OF THE LUNG.**—Benign growths of the lung are so exceedingly rare and so lack-

ing in clinical significance as to be negligible. Of the malignant growths the differentiation between sarcomas and carcinomas has only a pathological and no clinical interest. Most malignant growths of the lung are secondary to similar disease in other parts. They may result from metastasis, either lymphogenous or hematogenous, or be due to extension from contiguous disease. The secondary growths most commonly occur as diffused nodules scattered through both lungs. Primary growths are rare. Cancer is more frequent than sarcoma both in primary and secondary cases. The primary growths are usually unilateral and may be quite extensive, invading a lobe or almost an entire lung.

Malignant growths in the lung generally cause symptoms early in their course, but these are unfortunately not characteristic. Pain, cough, expectoration, and dyspnea, and later the characteristic cachexia, are the main symptoms. Pain may indicate involvement of the pleura. The expectoration varies greatly in consistency. It may rarely contain fragments of the neoplasm, and its microscopic examination may thus clinch the diagnosis. It is frequently bloody. Other symptoms occur dependent on pressure on the great vessels and structures in the mediastinum. The physical signs are not typical, depending, of course, on the physical conditions of the growth and surrounding pulmonary tissue, but may be of great help in arriving at the diagnosis when taken in consideration with the other symptoms. Inspection may show bulging of the chest wall, defective expansion, and dilatation of the superficial veins.

Tumors of the lungs and pleura are divided by the writer into three major groups: those in which the tumors are metastases from distant organs; those in which they are extensions from neighboring organs, and those which are primary. Among the 10,829 autopsies performed in the Pathological Institute at Munich during the ten years from 1900 to 1909 1342 cases of tumors were found, 12.4 per cent.; of these, 184, 13.7 per cent., were of the lungs and pleura. Of the latter, 133, 73.4 per cent., were metastatic, 18, 9.8 per cent., were extensions from other organs to the lungs, and 31, 16.8 per cent., were primary.

In metastatic tumor operation is absolutely contraindicated. In cases of extension from neighboring organs the mortality attending operation is given as 53 per cent. Primary tumors are divided into the benign, including fibroma, chondroma, osteoma, dermoid cysts, and angioma, all of which are rare and of little surgical interest; sarcoma of the lungs, in some of which the prognosis of operative intervention may be said to be not unfavorable; sarcoma of the pleura, 10 cases of which are reported in literature, while only 1 was found among the 10,829 autopsies, 3 of the 10 proving operable; carcinoma of the lungs, the operability of which is estimated at 9 per cent., and carcinoma of the pleura, the operability of which is still less favorable. Seydel (*Münch. med. Woch.*, March 1, 1910).

Case of primary cancer of the lung. A comprehensive study of the question led to the following conclusions: Primary carcinoma of the lung is a rare affection, occurring approximately once in 1600 autopsies. Probably the majority of so-called cancers of the lung are in reality of bronchial origin. Squamous-celled cancers of the lung probably arise in the majority of cases from bronchial epithelium which has undergone a metaplasia. Henrici (*Jour. of Med. Research*, July, 1912).

Diagnosis of malignant pulmonary tumors by the sputum. (*Betschart.*)

Fig. 1.—Fresh sputum, magnified 275 times. *a*, uninuclear, large, round cell; *b* and *b1*, round cells with several nuclei; *d*, red blood-corpuscles; *e*, free fat-globules; *f*, kernel cells; *m*, large cellular group.

Fig. 2. —Fresh sputum, magnified 275 times. *m*, group of cells.

Fig. 3.—Preparation of lung colored with borax-carminc solution, seen through microscope. *s*, carcinomatous tissue; *m*, lung-tissue.

Fig. 4 —Lung-tissue, magnified 275 times. *a* and *b*, alveoli filled with cells having one or several nuclei.





The **diagnosis** of malignant growth of the lungs in primary cases is difficult. Thoracentesis will usually aid, and cancer cells may be found in the fluid withdrawn, which is usually bloody. Intrathoracic aneurisms cause many symptoms similar to cancer of the lung and must be carefully excluded. Enlargement of the supraclavicular lymph-glands is of fairly constant occurrence in malignant disease.

Microscopic diagnosis (see the annexed illustration) is sometimes possible by examination of the sputum. Bronchoscopy is also useful when the growth involves the larger bronchi. The X-rays are elucidative in most cases.

Of 21 cases of primary lung carcinoma studied at autopsy, 13 had been radiographed during life. The X-ray examinations show that the development of lung carcinomata varies greatly. Usually the growth involves a whole lobe; but with almost equal frequency, the neoplasm starts as a small focus at the hilus, surrounded by similar foci in the immediate neighborhood. Finally, there is the type characterized by multiple foci of carcinoma scattered throughout the lung.

In the differential diagnosis of primary lung carcinoma, the following conditions must be taken into account: the various other types of mediastinal tumor, aneurism of the aorta, tuberculosis, gangrene, lung abscess, chronic fibrous pleurisy, and bronchiectatic cavities. Carcinoma very seldom affects the upper lobe of the lung. Otten (*Fortschr. a. d. Gebiet. d. Röntgenstrahlen*, Bd. ix, H. 6, 1906).

Case in which a carcinoma was located with the Roentgen rays and directly inspected by bronchoscopy. It was in the right main bronchus and finally involved the superior vena cava. Schrötter (*Zeit. f. klin.*

*Med.*, Bd. xlii; Schötter *Festschrift*, 1907).

Gerhardt gives sound advice when he bids us suspect of pulmonary cancer every elderly person who had bloody expectoration, and where heart disease and tuberculosis can be excluded. No age, however, is exempt, and our suspicions should at all times be readily aroused. When a study of the sputa, the X-rays, the bronchoscope, and all the other diagnostic means fail to assure the diagnosis, an exploratory thoracotomy would be indicated. I. Adler (*Can. Prac. and Review*, July, 1909).

Case of carcinoma secondary to cancer of the breast in which the character of the signs assisting in the differentiation of this condition from pulmonary tuberculosis was atypical. In this case there was absence of emaciation, but great dyspnea and cyanosis. The most suggestive feature was the peculiar resistance felt during percussion, but this, of course, could be of no value for the early recognition of cancerous lung involvement. Hoyt (*Arch. of Diag.*, Jan., 1912).

Tuberculous inflammation and cancer may exist conjointly in three forms: 1, the cancer may dominate, infiltrate the tuberculous granulation tissue, and prevent a successful invasion of the tuberculous infection; 2, the tuberculous inflammation may overgrow and destroy the cancer; 3, there exists a close association of the two diseases—symbiosis—without any appreciable influence of one upon the other. Finally, all observations collected from literature excepting one agree that caseation puts a stop to all cancerous invasion, due, no doubt, as Borst and others have pointed out, to unfavorable nutritive conditions. Oertel (*Jour. Med. Research*, Feb., 1912).

**Treatment.**—Medical treatment is, of course, of absolutely no avail, and the only hope for these cases in the present state of knowledge

concerning the origin of new growths lies in early surgical intervention, described farther on in this section. Multiple secondary growths are, of course, hopeless, the only treatment being the prophylactic removal of the primary growth. The primary growths, when single and not too extensive, if recognized early, it may reasonably be hoped, might be successfully removed by a pneumectomy, *q.v.*

A comprehensive experimental research on cats, dogs, goats, and sheep and two clinical experiences showed the writer that, by shutting off part of the lung from the circulation by ligating its arteries, intense proliferation of connective tissue follows, the part of the lung involved becoming a hard, tough mass. There is no doubt of the advantages it offers as a preliminary to resection of a tumor in the lung or a plastic operation on the thorax. Schumacher (*Archiv f. klin. Chir.*, Bd. xcv, Nu. 3, 1911).

**BRONCHIECTASIS.**—While properly speaking a disease of the bronchi, the surgical aspects of this condition may be treated here briefly. The disease has for a pathological background a purulent inflammation of portions of the bronchial tree, associated with dilatation of the bronchi into tubular or saccular cavities. It is not believed that diseases inducing severe coughing are in themselves sufficient to cause the dilatation of the bronchioles existing in bronchiectasis. In addition to the strain there must be disease of the walls of the bronchioles, which destroys or lessens the resistance of their supporting tissue, muscular and elastic fibers, and cartilage. Influenza is the disease most frequently preceding the development of bronchiectasis.

It is also an occasional sequela of pneumonia, bronchitis, tuberculosis, whooping-cough, and measles.

**Symptoms.**—The most important single symptom of bronchiectasis is the paroxysmal cough, coming on upon change of posture, as on getting up in the morning, and bringing up large quantities of a yellowish, mucopurulent sputum. In cases of some duration the sputum and breath take on a horrible fetid odor. The physical signs are, as might be supposed, very variable. The signs of importance are those of cavity formation.

**Treatment.**—Surgical treatment is rarely resorted to for obvious reasons. It can, of course, do no good in cases of diffuse bronchiectasis. Its field of usefulness lies in those cases with one or a very few large cavities near to the surface of the lung, especially when walled off by pleuritic adhesions. Here incision and drainage offer the best hope for recovery. See also page 672, vol. ii, for cases in which drainage or resection were resorted to.

**Ligation of branches of the pulmonary artery** for bronchiectasis, as shown by Sauerbruch and Bruns, causes subsequent shrinking and connective-tissue proliferation in the lung.

Personal case of a young man 17 years of age in whom the writer ligated the branches of the right pulmonary artery that ran to the middle and lower lobe on that side. The patient was kept in a slight Trendelenburg posture for two days prior to operation, so as to have him cough up as much as possible of the retained secretion. One hour before operation he was given 8 minims (0.5 c.c.) **Magendie solution** plus  $\frac{1}{150}$  grain (0.0004 Gm.) of **atropine**. The negative chamber was used. The

operation was done under regional anesthesia, **novocaine** and **suprarenin** being injected into the fourth to the eighth thoracic nerve near the spine; then the field of operation itself was anesthetized and prepared.

The patient stood the operation nicely. He was returned to the ward and made an uninterrupted recovery. He was out of bed on the fifth day. An effusion into his pleural cavity proved to be sterile on bacteriological examination. The patient has very much improved since the operation, and the amount of expectoration has become reduced from ten to twelve ounces to less than one ounce. Willy Meyer (Med. Rec., June 22, 1912).

After treating 26 cases the writer concludes that palliative treatment should be restricted to hopeless cases, extensive unilateral or bilateral involvement, adhesions, etc., that render extirpation impossible. A single focus, or multiple foci in 1 lobe, should be removed surgically. Even when an abscess has extended so as to implicate neighboring lobes in one single infected mass, extirpation may be performed successfully. Lillenthal (Annals of Surg., July, 1916).

The writer operated on 4 patients who had been given systematic internal treatment for more than a year in vain. All were greatly benefited or clinically cured by the **subperiosteal resection** of from 13 to 20 cm. of 4 or 5 ribs, suturing in 2 tiers with a compressing pad above. One patient was thus completely cured in 5 weeks from a year's disturbances from profusely secreting fetid bronchiectasis. There was some persisting pain in the region for a time, but this gradually wore off. He advises subperiosteal resection first, and only if this proves inadequate, removal of the periosteum and intercostal muscles, supplementing the operative with internal measures as required. J. H. Zaaier (Neder. Tijdsch. v. Geneeskunde, Feb. 19, 1916).

In a report of 5 complete **resections of the lower lobe of the lung**, with one death, the writer concludes

as follows: 1. Advanced bronchiectasis cannot be cured by medications, inhalations, intratracheal injections, intratracheal irrigations, climatotherapy or vaccines. 2. Collapse therapy produced either by nitrogen, artificial pneumothorax or by surgical measures is not curative. 3. Pulmonary arterial ligation is of more definite value as a preparation for lobectomy than as a curative measure *per se*. 4. Excision of the diseased portion of 1 lung is the only curative treatment of advanced bronchiectasis. S. Robinson (Surg., Gynec. and Obstet., Feb., 1917).

**PERICARDITIS.**—Pericarditis is classified as acute and chronic, and as primary and secondary. The absolutely primary cases, the so-called idiopathic pericarditis, are exceedingly rare, and the differentiation between acute and chronic cases is of little clinical significance.

Infection of the pericardium may be the result of trauma in the shape of blows over the heart or of penetrating wounds from without or within. Penetrating wounds from within result from the perforation of the pericardium from the esophagus by sharp objects, as spicules of bone. Pericarditis occurs in practically all acute infections as a complication of varying rarity. It occurs with greatest frequency during or following acute articular rheumatism and chorea, pneumonia, pleurisy, tuberculosis, and ordinary septic infections. Pericarditis during acute gonorrhea should be more frequently kept in mind.

Pericardial inflammations correspond most accurately in their pathology to inflammations of the pleura. Fibrinous, serofibrinous, seropurulent, and purulent forms all occur, and a more or less hemorrhagic tendency is not infrequently observed. In cases going on to recovery the fluid

portion of the exudate is absorbed readily, the fibrinous with difficulty, and pericardial adhesions frequently result from its organization. The great danger lies in involvement of the myocardium, which causes more serious trouble than the mechanical effect of the presence of the exudate. (See also the article on Pericarditis.)

**Symptoms.**—The symptoms of pericarditis are in the majority of cases masked more or less completely by those of the primary disease. Pain in the precordium or bulging may attract attention. The general symptoms are those of the underlying disease or of any infection. The physical signs are: bulging of the chest wall in children and young adults, considerable increase in the area of cardiac dullness, and in the early stages of the disease the to-and-fro friction rub of the inflamed and fibrin-covered pericardium. Later, after exudation, the heart sounds may have a muffled, far-away character.

**Diagnosis.**—In diagnosis the differentiation between cardiac dilatation and pericardial effusion gives the most difficulty, and mistakes are made quite frequently. The area of dullness extends more to the right, especially in the fifth interspace, and above may extend upward over the third costal cartilage in pericardial effusions. Change in the area of dullness with change of position is, of course, of great value. The cardiac impulse is usually perceptible in dilatation, frequently absent in effusion.

**Treatment.**—The tolerance of the pericardium to surgical manipulation is now well established. **Paracentesis** as a diagnostic and therapeutic procedure in serous effusions has proved its value, and when carefully

done under aseptic precautions is little, if at all, more dangerous than the same operation on the pleura. Incision and drainage in cases with purulent exudate offer the only chance for recovery. These procedures will be considered under operations on the heart. In certain cases of chronic pericarditis **pericardiectomy** has been recommended.

A study of 300 articles on the operative treatment of pericarditis showed that **puncture** is allowable only when there is no suppuration, which can be determined by an exploratory puncture. In case of suppuration, **resection of ribs** and **pericardiotomy** only can be considered. After pericardiotomy the pericardial cavity should be carefully rinsed with **salt solution** and extensively drained. In case of chronic adhesive mediastino-pericarditis Brauer's technique of **cardiolysis**—osteoplastic resection of the wall of the thorax to release the adherent pericardium—has proved a life-saving operation and is evidently destined to play a prominent part in the treatment of this affection. E. Venus (Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Aug. 6, 1908).

**EMBOLISM AND THROMBOSIS OF THE PULMONARY ARTERY.**—Several recent attempts at the removal by surgical means of the thrombi from the pulmonary artery having been made, it becomes necessary to consider this condition briefly here.

In a study of 1200 autopsies the writers found that spontaneous thrombosis is much commoner than embolism, in the proportion of 8 to 1. An unaccountable acceleration of the pulse or respiration rate, beginning in the second week after a major operation, especially abdominal, and associated with slight pyrexia, suggests the possibility of spontaneous thrombosis and of a sudden fatal termination about the

third week. Cases of spontaneous thrombosis are overlooked from the assumption that only embolism can cause death in a few minutes, from neglect to remove and harden the heart and lungs, together, and trace the disturbance of the thrombi *in situ* in properly hardened specimens, and especially from neglect to make a thorough microscopic examination. Glynn and Knowles (Brit. Med. Jour., Nov. 5, 1910).

A comprehensive study of cases at the Mayo Clinic showed that many deaths supposed to be due to surgical shock are in reality due to pulmonary fat embolism and its attendant blood-pressure phenomena. A lowering of arterial blood-pressure is caused with an elevation of venous blood-pressure which may be sufficient to cause death. Intravenous infusions, therefore, are contraindicated because of the increase of pressure on the right heart. Pulmonary fat embolism is simply demonstrated at autopsy by proper, careful, excavation of the whole chest contents through the mural, ventral opening without severing the great vascular channels. The writer during 8 months observed 6 instances of fatal postoperative fat embolism in the necropsy service of the Mayo Clinic. Three of these followed breast amputation; 1, ventral herniotomy; 1, craniotomy for brain tumor; and 1, laminectomy for spinal cord tumor. Bissell (Surg., Gynec. and Obstet., July, 1917).

Embolism and thrombosis give rise to practically the same symptoms, and, since thrombotic changes occur around the embolism after its lodgment, the two conditions are best considered together. Pulmonary embolism is not a very rare occurrence as a sequela to thrombotic lesions of the peripheral veins, especially those of a septic character, of which puerperal sepsis may be taken as a type, and in which it is quite common. The process may occasionally be regarded

as the extension of similar conditions from the right side of the heart. The symptoms depend upon the size of the vessels occluded and upon the suddenness and effectiveness with which the circulation is shut off. Occlusion of the main trunk or a large branch is one cause of sudden death. In other cases, even though the main trunk be the site of the lesion, the occlusion may be gradual and partial. Here pain, cyanosis, and dyspnea, of rather sudden origin, followed by expectoration of blood-tinged, frothy mucus, would be suspicious. Respiration is greatly increased in rate, and there is a marked sensation of oppression in the chest. The diagnosis usually rests on the presence of a predisposing cause, venous thrombosis elsewhere, or cachectic and anemic states, typhoid fever, influenza, puerperal sepsis or other predisposing disease, associated with sudden onset of severe respiratory phenomena.

Pulmonary embolism, though nearly always due to a blood-clot, is due in rare instances to other bodies, such as hydatid cysts. It may originate in a capillary, a hydatid, or even a scolex being arrested, and forming the starting point of a cyst; the embolism may then pass unperceived, and the signs be those of hydatid of the lung. If the hydatid be larger, the embolism invades a main trunk. The writers have collected 12 cases of this kind. In some instances it follows rupture of a cyst on the liver, and the symptoms are the usual ones of serious pulmonary embolism, but occasionally there are special symptoms, as in the writers' case—a man of 42 who had a hydatid cyst of the myocardium, which ruptured into the right ventricle, and produced embolism of the left pulmonary artery. The patient survived for ten days. There was sudden, severe pain in the chest, great

dyspnea, increased frequency of respirations, crepitations at the left base, and a temperature of 40.3° C. Pneumonia was diagnosed. At the autopsy there was no consolidation, but much edema and congestion. A hydatid cyst was found free in the left pulmonary artery without blood-clot. Garnier and Jomier (*Presse méd.*, June 14, 1905).

Postoperative embolism affects the pulmonary artery and its branches in the majority of cases. Normal blood does not coagulate in normal vessels, and an embolus presupposes a thrombus from which it is detached. For the formation of a thrombus there must be fibrinogen and calcium salts, which are normal to the blood, and a nucleoproteid, which is never in normal blood, being formed by the degeneration of blood-plates and leucocytes. Anemia, chlorosis, sepsis, excess of calcium salts, slowing of the blood-current, traumatism, inflammation of the walls of the vessels, pressure, and many other conditions may predispose to the formation of thrombi; conditions which call for operative measures frequently involve one another of the foregoing causes. Thus, fibroid tumors, which are most frequently followed by thrombosis and embolism after their removal, may be said to predispose to such complications, owing to their frequent coincidence with excess of calcium salts in the blood, degeneration of the heart muscle, consequent imperfect contractions, and residual blood, with retardation of the blood flow and predisposition to heart clot. The latter condition has often been observed in the right side of the heart, and is followed by fatal embolus in the lung.

Signs of impending thrombosis are weakness and rise in the pulse and temperature. Precautionary measures for the prevention of abnormal coagulability of the blood consist in the use of abundance of alcohol and citric acid, the withholding of milk, the avoidance of hemorrhage at the

operations, so far as possible; also the avoidance of motion and excitement after the operation. When pulmonary embolism occurs, oxygen should be freely administered. E. Boise (*Amer. Gyn. Soc.; N. Y. Med. Jour.*, July 14, 1906).

The prognosis is, of course, exceedingly grave, particularly in involvement of the main trunk or the large branches. Here the outcome is with great uniformity fatal. These are the very cases which are susceptible of a possible successful surgical intervention.

A large percentage of the lung affections observed after laparotomy are due to embolism. Experiments on 40 rabbits gave, after laparotomy, an embolic lung affection in 12, and an embolic pneumonia in 4. Embolism, therefore, should be regarded as an important factor in the development of lung complications after abdominal operations. About a third of the lung infarcts are followed by pneumonia. Infection is indispensable, but this may occur primarily with the embolus or may follow later. Mikulicz's 143 cases of pneumonia following 1781 laparotomies gave a mortality of almost half. The writer reports 77, or 6.43 per cent., cases of pneumonia following the laparotomies between 1892 and 1902. Out of the 77 cases 14 (1.17 per cent.) were of embolic origin, and 8 were suppurative pneumonia. Gebele (*Beiträge z. klin. Chir.*, Bd. xliii, Nu. 2, 1905).

The writer's personal experience of 8 fatal cases of pulmonary embolism after gynecological operations in the last nine years emphasizes the desirability of ligating all veins before opening organs which are certain to contain bacteria, such as the vagina. By ligating the veins while the hands are still aseptic, the danger of infection, and of subsequent thrombosis with embolism, is very much diminished. These emboli, at least, which are traceable to bac-

terial invasion, will be avoided. J. Veit (*Zentralbl. f. Gynäk.*, Jan. 1, 1910).

Stadelmann (*Deutsche medizinische Woch.*, June 24, 1909) has shown the possibility of the bronchial arteries substituting for the pulmonary when the occlusion of the latter has come on slowly.

**Treatment.**—Operation for embolism of the pulmonary artery was resorted to by Sievers and again by Trendelenburg in 1908. The following description is taken from Trendelenburg's report in the *Deutsche medizinische Wochenschrift*, July 2, 1908:—

An incision was made along the left border of the sternum from the upper border of the first rib downward to that of the third rib. A horizontal incision was then made from the first incision along the left second rib, and the two triangular flaps thus made were turned back. The second rib was resected near the sternum, the pleura being opened, and the pericardium was opened at the upper border of the third rib. The aorta and pulmonary artery were held forward by a large bent probe until a rubber tube could be passed around them. These vessels then ceased to pulsate, while the heart contracted weakly and irregularly; just then breathing ceased, and there was not time enough to separate the pericardium from the pulmonary artery; so the rubber tube was drawn up so as to control the pulmonary artery, the latter was opened with a knife, polypos forceps introduced, and a thrombus 34 cm. long was withdrawn. Three more thrombi were withdrawn, but not so long as the first. Blood now began to flow from the artery,

and the wound was closed with forceps and the rubber tube was relaxed. Artificial respiration became necessary and soon had respiration and circulation going again. Some trouble was experienced in suturing the wound in the pulmonary artery on account of its strong pulsation, but it was done by drawing the artery forward by means of the rubber tube until a silk suture could be passed and tied, then the tube was relaxed and the artery permitted to pulsate a while, this procedure being repeated until the suture was completed, then the tube was removed and the wound closed. Death occurred thirty-seven hours after operation. No recoveries have been reported.

### TRAUMATIC ASPHYXIA.

This condition, or stasis cyanosis of the head, or, again, pressure cyanosis of the head may follow sudden severe and long-continued compression of the chest suspending respiration, as being caught between an elevator and some other object or being squeezed by a crowd in a panic. The venous blood is forced back into the veins and capillaries, dilating them or even causing rupture and extravasation.

The veins of the head and neck being provided with incompetent valves as compared with those of the extremities, the result of the pressure is seen chiefly in the head, neck, and conjunctivæ.

In the white race the discoloration is seen as a purple or reddish blue in the skin of the scalp, face, neck, and sometimes extending slightly down the chest. The conjunctivæ are also affected, hemorrhage usually occurring here. The skin is swollen slightly. In colored persons the dis-



coloration may be difficult to recognize, but the swelling of the skin, the subconjunctival hemorrhage, and the history of the injury should lead to a careful examination. In a case seen by one of us in a negro there was no difficulty in detecting the cyanosis of the skin.

Sometimes hemorrhage occurs in the skin, but in many cases it would seem that only a dilatation of the capillaries takes place, Beach having examined with the microscope pieces of skin excised from the neck and found them normal. His case, shown in the annexed colored plate, graphically illustrates the condition. The case itself is described below.

The writers found but 6 cases of traumatic asphyxia in literature—three boys about 15 years of age, the others, including the writers' case, being young adults between 22 and 36 years old. In all of these the dominant and diagnostic feature was the blue-black discoloration of the skin, mainly confined to the face and neck above the clavicle; in one the discoloration extended into the forearm for some distance, and in another it extended over the chest wall to the second or third ribs.

The writers' case was a large, muscular German aged 30 who had been caught and held by a moving freight elevator. The elevator was stopped, and the man released in from three to five minutes. While this was being done his face became black, blood ran from his nose and mouth, and his eyes protruded. He was unconscious for a few minutes after being released. Recovery followed, the discoloration disappearing steadily after the third day.

In some cases there appear complications, with pyrexia, bloody expectoration, and labored breathing. This condition Perthes called a "contusion pneumonia"; it may be expected to subside rapidly and not to result

fatally. Beach and Cobb (*Annals of Surg.*, April, 1904).

Report of a personal case and 18 other cases found in literature. Not only may the air be prevented from entering the lungs by their inability to expand, but the contents of the thoracic vessels may be forced out, and, in the case of the veins, the current is reversed, overcoming the valves and damming the blood back into the capillaries. If the force acting is sufficiently great, it is conceivable that the capillary vessels would be dilated to a point where paresis would ensue. The treatment of this condition is directed to the re-establishment of respiratory function, such as **artificial respiration, oxygen inhalations, atropine, and strychnine**, and when the right side of the heart is dilated **venesection**. Despard (*Annals of Surg.*, June, 1909).

Case of traumatic asphyxia in a man 23 years old who had had one former attack similar to this one five years before. One hour before admission the patient became unconscious and fell, while operating a moving-picture machine. The unconsciousness lasted for only a few moments. When the ambulance arrived he was conscious, but confused, and answered questions slowly. After his fall, the onlookers stated that his face became dark blue.

Upon his arrival at the hospital there was very deep cyanosis, extending as far down as the level of the thyroid cartilage. There was a scalp wound and hematoma over the right parietal region, and an incised wound in the forehead, evidently due to the fall. There was bleeding from both ears, a large, subconjunctival hemorrhage in both eyes, and bleeding from both nostrils.

The hematoma was incised and the skull exposed without finding any external evidence of fracture, and there were no focal signs indicating an intracranial injury. While the hemorrhages noted above suggested a fracture of the base of the skull,



Traumatic Asphyxia. (*H. H. A. Bzack*.)



the patient's rapid improvement dispelled that idea.

The patient having had a similar attack five years before, which also came on spontaneously, the writer regards the case as one of traumatic asphyxia due to epilepsy, cases of which have been reported. The patient's cyanosis gradually disappeared, the subconjunctival hemorrhages were absorbed, and he left the hospital within a week, apparently in perfect health. Parker Syms (*Annals of Surg.*, Aug., 1911).

The discoloration, or cyanosis, usually fades away in three or four weeks, except that in the eyes, which requires a longer time. In bad cases there may be hemorrhages from nose, mouth, and ears simulating fracture of the base of the skull. It would seem that the prognosis is good in those who recover consciousness. According to Ruppanner, the prognosis is good in every respect except as to vision, optic atrophy and opaque patches on the macula having been reported.

The writer depicts the effects of a stampede from a moving picture theater after a cry of "fire" had been raised. The injury usually produced by pressure on the abdomen and chest of sufficient duration to cause cessation of respiration lasting some time. The patient may be unconscious and show cyanosis of the scalp, face, neck and chest down to the third or fourth rib anteriorly. The lips and tongue may be somewhat swollen, and together with the mucous membranes exhibit the same purplish tint as the skin. The discoloration extends just over the prominence of the shoulders, and for a short distance down the back, sometimes even outlining the double triangle of the lower portion of the trapezius muscle. Robertson (*Can. Med. Assoc. Jour.*, June, 1914).

While the best of resuscitation apparatus provide mechanical means of

artificially supplying air, or air slightly enriched with oxygen, to the lungs, the danger from their use lies in the fact that too much reliance is placed upon their efficiency, and thus too often the victim is neglected while the apparatus is being brought. The most important element is **prompt action** and there should be universal training in the technique of the prone pressure manual method of artificial respiration. In *gas and smoke cases* **oxygen** should be administered at once and the only effectual method for this is by means of a closely fitting mask and a distensible rubber bag. Yandell Henderson (*Jour. Amer. Med. Assoc.*, July 1, 1916).

## DISEASES OF THE CHEST WALL.

**PERIOSTITIS AND OSTEO-MYELITIS.**—The ribs and sternum are rarely the site of acute infections. The most frequent form is that occurring during or following typhoid fever. Ordinary septic osteomyelitis is rare. The symptoms are the usual ones of pain, great tenderness, swelling, and occasionally hyperemia of the skin over the affected bone. Fever is usually present. The course of the disease is very variable, particularly the typhoid variety. This form may subside spontaneously or it may go on to suppuration and necrosis. The tendency is toward recurrence and chronicity. Surgical intervention in the shape of exposure and thorough removal of the diseased area, with provision for drainage, is indicated early.

Chronic inflammatory conditions here are usually either tuberculous or syphilitic, and are more frequent than the acute inflammations.

The tuberculous form frequently is seen as a periostitis. In a great many cases a history of traumatism is given. Its sites of election are the

costochondral junction, the costal cartilages, or the chondrosternal junction. The first symptom noticed is very often the elongated, soft, sausage-shaped swelling along one or more ribs. The subjective symptoms are mild and may be wanting entirely, pain, for instance, being entirely lacking. The destruction of tissue results in the formation of cold abscesses in a large percentage of the cases. These may burrow in the soft parts externally or between the pleura and the ribs. Fortunately a rupture into the pleural cavity is rare. The symptoms of the syphilitic form are similar to those of the tuberculous and their clinical differentiation is difficult.

In the treatment of these conditions **fresh air** and proper **hygiene** in the tuberculous cases and **mercury** and **potassium iodide** in the syphilitic are, of course, essential. In the presence of necrosis and the formation of cold abscesses the removal of the dead tissues is indicated.

**NEW GROWTHS.**—Among the benign growths found superficially in the chest wall the most frequent are lipomata, usually seen on the back. Hemangiomata, lymphangiomata, cysts, wens, etc., all occur. Primary carcinomas of the skin of the chest are occasionally seen. Usually they are secondary to carcinoma of the breast. The treatment of any of these conditions is in no wise different from that of the same growths elsewhere.

Simple osteomata and chondromata of the ribs and sternum are generally seen at the costochondral or sternochondral junction. They may follow injury and are unimportant save in their differentiation from sarcomata.

The most frequent new growths of the ribs and sternum are the sarcomata. The condition is usually primary, but in a few cases is secondary to sarcoma of the pleura or lung. Trauma is mentioned as an etiological factor in the primary varieties. The site of election is the costochondral or sternochondral junction. Enlargement at this point, when rapid in growth, should always be regarded with grave suspicion, and the seriousness of the condition is ample justification for early and radical procedures to enable a microscopic diagnosis to be made. Occasionally these sarcomatous growths pulsate to such an extent as to simulate aneurism. The tendency to dilatation of the superficial veins over the tumor should be noted.

The prognosis in these cases is uniformly grave, and the only hope lies in early and radical excision of the bones involved. Death being otherwise certain, many chances must of necessity frequently be run. In many instances, however, the diagnosis is not made until the case is hopelessly inoperable.

**FRACTURES OF THE STERNUM AND RIBS.**—Fractures of the sternum are among the rarest of fractures, and, while any variety of fracture may occur in this bone, the most common is a transverse fracture at the junction of the manubrium with the gladiolus—in some cases a true diastasis. The cause is usually indirect violence, such as forcible flexion or extension of the body or strong muscular contraction.

The symptoms depend on associated injury to internal organs or to other bones, as the vertebræ, and may be cough, bloody expectoration, dysp-

nea, and interference with the heart's action. Crepitus, false point of motion, and overriding may be detected, the lower fragment usually resting on the anterior surface of the upper fragment.

Reduction may be effected by pressure with or without hyperextension of the body over a pillow. Should this fail and pressure symptoms exist, an incision should be made and the fragment pulled or pried into place.

Fractures of the ribs are among the most common of all fractures, from 9 to 16 per cent. of all fractures being of the ribs. The longest ribs, about the seventh, are most likely to be broken, and the point of fracture is most likely to be just about the angle. The injury is most common in adults in whom the ribs have lost their resiliency. Children are often run over by heavy wagons, the wheels passing over their chests without causing fracture of the ribs.

Fractures of the ribs are often multiple; they are usually simple, but may be compound by penetration of the skin or more commonly from penetration of the lung.

The causes are direct or indirect violence and muscular action. A blow or kick on the side of the chest may break one or more ribs. A compressing or squeezing force applied to the chest is more likely to break several ribs and to break them on both sides. Trivial forces sometimes cause fracture—probably because of pathologic changes in the ribs, such as an ordinary embrace, parturition, sneezing, or coughing.

**Symptoms.**—The symptoms are pain, tenderness, sometimes crepitus, abnormal point of motion, and cough.

The pain is increased by deep breathing, and the patient's breathing is shallow. Tenderness is often well marked over the point of fracture. Crepitus may be felt by placing the hands flat on the chest wall while the patient breathes. An abnormal point of motion or an offset or depression may be felt by following a rib carefully from end to end. If only one rib is fractured or even more, if the periosteum holds there is so little displacement that it may be impossible to detect it, the unbroken ribs acting as splints to prevent displacement.

As complications may be wounding of the pleura, lung, heart, diaphragm, or abdominal organs by fragments of the broken ribs or by the same force which broke the ribs. Wounding of the pleura may be indicated by hemothorax; of the lung by hemothorax, pneumothorax, emphysema, hemoptysis—one or more or all four; of the heart by symptoms characteristic of wounds of that organ, as rapid, embarrassed action, muffling of sounds, etc.

Emphysema is due to the escape of air or the forcing of air into the connective tissue, in the lung, beneath the skin, or elsewhere. While it usually means a fractured rib with wounding of the lung, it is not necessary to have a fractured rib in order to have emphysema. One of us has seen two cases of external emphysema following injury to the chest, both in children, in which repeated and careful examination failed to detect a fracture. Others have observed the same phenomenon. The lung may rupture without fracture of a rib, especially in children, and the air may be pumped or forced into the connective tissue, probably first ap-

pearing beneath the skin about the neck and thence extending perhaps to the entire subcutaneous tissue, making the patient appear like a blown-up rubber doll.

**Treatment.**—In the treatment of fractured ribs the indications are to reduce displacement, limit mobility, and attend to any complications which may exist. Seldom is it necessary or possible without operation to set a fractured rib. Partial rest is given by the application of adhesive plaster to the affected or both sides, if necessary, in order to diminish the respiratory excursions of the chest wall. Shave the chest and dry the skin. Cut strips of adhesive plaster about 3 inches wide and long enough to extend from the median line behind to the median line in front; or in bilateral fractures, to encircle the chest. Begin below, over the tenth rib, and apply each strip during expiration when the chest is smallest and continue upward to the axilla, each strip overlapping the one below to the extent of about one-third. After a week's rest in bed the patient is often able to walk about during the six or eight weeks of his convalescence.

Collections of blood and air, one or both, in the pleural cavity usually disappear in a few weeks. Large collections might cause dyspnea, or the escape of much blood might endanger life and require thoracotomy, the liberation of air and blood and the arrest of hemorrhage by ligation, suture, or compression with gauze packing. If the blood remains in the pleural cavity beyond a reasonable time, say six weeks, it may be removed by aspiration. Occasionally, emphysema follows hemothorax.

Emphysema seldom requires treatment, usually disappearing by absorption within a week or two. Sometimes, however, air is forced into the connective tissue of the lung by the respiratory act in such large quantity as to cause compression of the lungs and endanger life. **Multiple punctures** or even a **thoracotomy** may be required.

A broken rib end buried in a lung or other viscus should be removed.

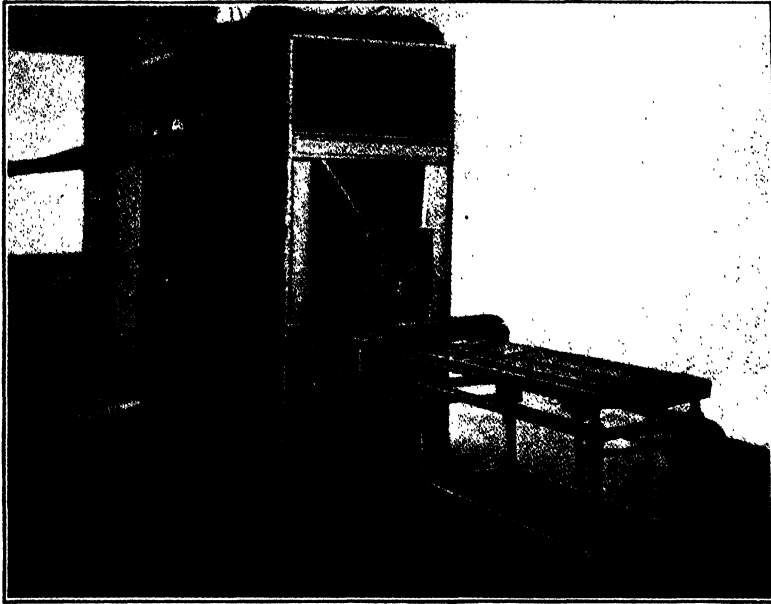
### OPERATIONS ON THE CHEST.

One of the dangers in operations on the contents of the thorax—though shown by the war to be less grave than formerly believed—is collapse of the lung as soon as the pleural cavity is opened; especially if both cavities are opened. Surgeons had long sought some method which would permit exposure of the lung without causing it to collapse. The methods which have been used in animal experimentation, and to some extent on the human patient, are as follows: (1) that by negative pressure; (2) that by positive pressure, and (3) that by differential pressure.

1. The **method by negative pressure**, as illustrated by Sauerbruch's cabinet, reduces the atmospheric pressure on the patient's exposed lungs by the amount of about 10 or 12 mm. of mercury, while the ordinary pressure of the atmosphere is preserved within the lungs. The cabinet is constructed of metal and glass, air-tight, large enough to contain a table for the patient's body, other necessary tables, and room for the surgeon and assistants. An opening is provided in one wall of the cabinet through which the patient's head projects into the ordinary atmosphere,

the opening being provided with a rubber collar which fits air-tight around the patient's neck. The air-pressure in the chamber is exhausted by a suction pump to the required extent—by reducing it 10 or 12 mm. of mercury. The anesthetist is outside with the patient's head. Later an anteroom, likewise air-tight and communicating with the chamber by an

increase of pressure required, while his body lies on a table in a room with ordinary pressure in which the operation is performed. The anesthetist is in the cabinet with the patient's head, and the pressure here is increased by a pump forcing air in until the manometer shows an increase of from 5 to 7 mm. of mercury. Neither patient nor anesthetist feels



Differential pressure cabinet; head rest removed. Patient's head projects out over table and is adjusted in collar of cabinet without changing position of body. (*Willy Meyer.*) (*Annals of Surgery.*)

air-tight door was provided and electric lights and telephones were established. Under these conditions both pleural cavities have been opened and operations performed without collapse of the lung—such as resection of the esophagus and esophagogastrostomy.

2. In the **method by positive pressure**, the conditions are to a great extent reversed. The patient's head is placed within a cabinet, air-tight and strong enough to stand the slight

any discomfort from this increased pressure, and the pleural cavities can be opened without lung collapse.

3. It seems that little has been done to make practical the **method by differential pressure**. This method might be accomplished by the union of the two cabinets used for the negative and positive pressure methods, placing the patient's head in the cabinet with positive pressure and his body in the cabinet with negative pressure; then, the greater the positive



pressure used, the less the negative pressure required, and *vice versa*, so that the desired result could be obtained by a less degree both of positive and negative pressure than if either were used alone.

**Meltzer and Auer's method** is based on the fact that, by ventilating a lung with a continuous current of air, respiration takes place in the absence of respiratory movements. They introduced a small-sized catheter into the trachea of the dog as far as the bifurcation and then passed a continuous current of air through it under low pressure. The air ventilated the lungs and escaped immediately to the exterior through the trachea. The animals could be kept in this condition for three or four hours or more, ether being introduced with the air. The writer operated on the thoracic aorta in 6 dogs, using a foot bellows to ventilate the lungs. In three experiments the upper part of the descending aorta was cut transversely and the ends united by a circular suture, necessitating an interruption of the circulation from three to six and a half minutes. The first 3 animals recovered without incident. In the fourth experiment the ascending portion of the aorta was cut longitudinally about 3 cm. above the heart and sutured. This operation involved two interruptions of the circulation, each lasting about thirty seconds. The animal remained in good health. The fifth experiment consisted in severing the ascending aorta in the middle and interposing between its ends a segment of a large jugular vein preserved in cold storage. The circulation was interrupted for seventeen minutes. The sixth experiment was done by temporary tubing of the aorta, in order to avoid medullary complications. The upper part of the descending aorta was laid open by a longitudinal incision and a paraffined tube inserted into its lumen and temporarily fastened. This involved only a brief interruption of the circulation, which

was immediately re-established, and it was possible to extirpate at leisure the anterior wall of the part of the vessel tubed and to substitute for it a segment of vena cava preserved in cold storage. The operation lasted twenty-four minutes. The tube was then taken out through a small incision in the outer wall, and normal circulation re-established. The animal recovered, but death occurred suddenly from hemorrhage twelve days later, due to a defect in the vein preserved in cold storage. These experiments, the writer says, prove that operations on the thoracic aorta need not be dangerous, but are as simple as abdominal operations by this method. Alexis Carrel (Jour. Amer. Med. Assoc., Jan. 1, 1910).

1. Intrathoracic surgery cannot be done properly and safely without **differential-pressure** apparatus.

2. Negative and positive differential pressure are, it seems, not identical in their effects on sick human beings. Whether they are or not must still be established, and indications be found for their use. This is rendered feasible by the universal differential-pressure chamber.

3. Continuous intratracheal insufflation, as practised by Meltzer and Auer, appears to be a positive differential-pressure system.

4. Its weak points are the use of the human trachea as a vital part of the apparatus; the possibility of aspiration at the beginning of the operation, with subsequent pneumonia, and of interstitial emphysema at the end of the operation, as a consequence of its employment; also the required deep anesthesia. Intubation reaching below the glottis has been found to give rise in the human trachea to immediate copious secretion of mucus.

5. Sudden complete interruption of the prevailing differential pressure, followed immediately by its equally sudden restoration, as practised in continuous intratracheal insufflation, is liable to hurt the human heart. Very slight changes in intrabronchial

pressure give rise to very great changes in blood-pressure.

6. Continuous intratracheal insufflation apparatus is not adapted for use in the after-treatment, nor is it otherwise all-sufficient. Those employing it need some other type of differential-pressure apparatus in addition to it, in order to be prepared for every emergency.

7. The safest method of general anesthesia is the one used in our everyday surgical work, the inhaling of the narcotic, with spontaneous respiration and with mouth and throat left unencumbered. This method is the one used in the larger differential-pressure chambers.

8. In surgery, when entrusting human life to the safe working of mechanical apparatus, it is wise to have substitutes on hand, in order to be prepared for accidents. In continuous intratracheal insufflation everything depends, at present, on the one cannula and the patency of the trachea.

9. So far as the patient is concerned, a differential-pressure system leaving mouth, throat, and trachea unencumbered appears preferable to one requiring intubation. Willy Meyer (*Med. Rec.*, March 19, 1910).

The dangers from opening up the thoracic cavity can be obviated in animals by mechanical means to prevent the diaphragm from making excessive excursions. Traction on the manubrium before opening the chest has this effect; hence traction on the costal arches on both sides may prove effectual in man. After the chest is opened, the writer presses the bulging diaphragm downward with the tip of his little finger, or a spatula, repeating this rhythmically; the respiration becomes slower and regular at once. H. Teske (*Zentralbl. f. Chir.*, Jan. 28, 1911).

The **Meltzer and Auer apparatus** consists of a foot bellows, a Wolff bottle, a mercury manometer, and a soft-rubber catheter, so connected by rubber tubing that a current of air

may be forced through ether in the Wolff bottle and through the catheter into the lungs. The manometer is so attached that the pressure under which the air and ether current is maintained may be read in millimeters of mercury. The technique is as follows: The patient is anesthetized in the usual way, and the pharynx sprayed with 10 per cent. cocaine solution. With the head extended over the end of the table, and the tongue pulled forward, the forefinger of the left hand holds open the glottis while the right passes into the trachea a soft-rubber catheter. At first this is difficult, but with a little practice it can be accomplished without the aid of instruments. The catheter should be of a diameter about one-third that of the trachea. A catheter too large causes shallow breathing, and cyanosis under small pressure, and one too small will fail to keep the patient under. For the average adult a catheter from number 22 to 28 French will be the correct size. The catheter is passed down to within one inch of the bifurcation, which measures on the catheter about 26 cm. from its tip. The bellows is then attached, and a mixture of air and ether is pumped in a steady stream into the trachea under about 12 mm. of mercury pressure. The catheter partially obstructs the outflow of the air and ether, and therefore raises the intrathoracic pressure. When the thorax is open the lungs may be collapsed or distended at will by decreasing or increasing the pressure as read on the manometer. Normal respiration goes on as usual, becoming shallower as the pressure is raised. H. H. Kerr (*Va. Med. Semi-monthly*, July 12, 1912).

All the foregoing views, are being in a measure, modified by the developments of the war in respect to exposure of the lung which is already being deemed by Duval, of Paris, and others, quite as free from danger as opening of the abdominal cavity.

Major Pierre Duval (see *Wounds of the Pleura and Lungs at the be-*

ginning of this article) has shown that the exposure of the lung and the removal from it of a foreign body is as safe as most other major operations, and not only enables us to remove the bullet but also to clean the pleural cavity of its contained blood clot. Shortly after the receipt of the injury, when reaction has occurred, ether is administered by the open method (an endotracheal apparatus is not necessary), and an incision 9 or 10 inches long is made over the fourth or fifth rib. About 6 inches of the rib is then removed, and after cutting the intercostal membranes the pleura is carefully separated with the fingers above and below for some distance, to mobilize it. The pleural membrane is then rapidly divided the full length of the opening and a rib spreader is placed in position rapidly and sprung open. The lung is then taken by a pair of grasping forceps and pulled to the wound. If these maneuvers are *done rapidly* the mediastinum is steadied before the pneumothorax has had time to work injury to the circulation. The lung can then be drawn out onto the chest, the bullet easily felt, the lung incised over the bullet, which is removed, and the incision closed by one or two fine catgut sutures. Blood clots are scooped out, the cavity is gently mopped and disinfected, if thought necessary, by ether (Duval) or perhaps by neutral solution of chlorinated soda. The lung is then replaced but still steadied by the grasping forceps and the pleura is closed. The muscles are next pulled together with catgut mattress sutures and the skin is sutured with silk-worm gut. No drainage should be introduced. Finally, the pneumothorax is emptied by aspiration. If it is determined not to search for the bullet, aspirate the pleural cavity on the slightest suspicion of the onset of infection, and if coverslip smears confirm suspicion, the chest must be opened and drained. G. P. Müller (Trans. Penna. State Med. Soc.; Jour. Amer. Med. Assoc., Nov. 16, 1918).

**Paracentesis Thoracis, or Thoracentesis.**—This is the operation by which fluid is drawn from the chest by means of an aspirating needle or of a trocar and cannula; the former is generally preferred. The patient may be in a sitting or lying position, and the operation may be done without anesthesia or with a local anesthetic. The best place in which to insert the instrument is in the midaxillary line in the fifth intercostal space close to the upper border of the sixth rib. If there is much fluid in the pleural cavity and the diaphragm is depressed the sixth or seventh interspace may be used, but generally there would be some danger of entering the peritoneal, instead of the pleural, cavity. If it is desirable to avoid the entrance of air, a suction apparatus must be attached to the aspirating needle. The fluid should be withdrawn slowly, and the occurrence of violent cough, rapid pulse, or syncope is the signal to arrest the operation. The needle is withdrawn by means of a quick movement of one hand while the other instantly slides the skin so as to cover the opening between the ribs, where it is held until a little collodion or adhesive plaster is applied over the skin opening.

The accidents sometimes observed after puncture of the thorax, owing to the abrupt subsidence of the previous compression of the organs within, can be prevented by immediately allowing a certain amount of filtered air to enter. Fontana has done this with excellent results in 12 cases. EDITORS.

**Artificial Pneumothorax** has been advocated and made use of in **tuberculosis of the lung**, in bronchiectatic and other abscesses of the lung in which there are no pleural adhesions, and in **hemorrhage from the lung**.

Air may be used, but nitrogen is better, as it is more slowly absorbed (Murphy). A large aspirating needle connected with a reservoir of nitrogen by means of rubber tub-

ing (Amer. Jour. Med. Sci., April, 1912), who had tried it in 15 cases:—

"In order to insure complete anatomical recovery, it is generally agreed that the lung must be kept firmly compressed for about a year in uncomplicated cases be-

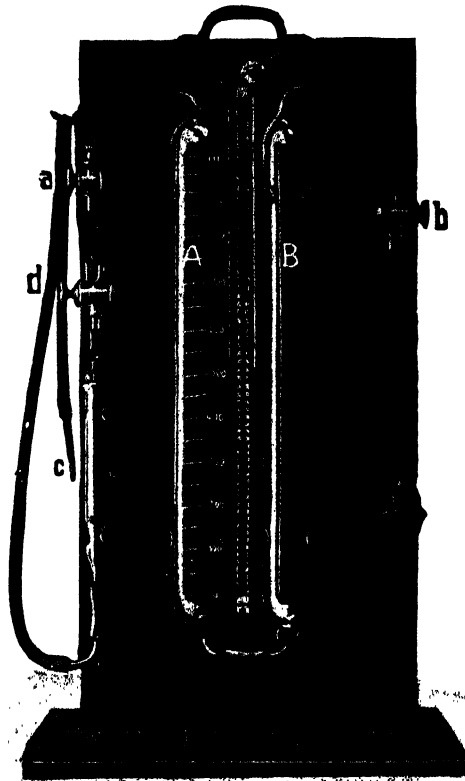


Fig. 1.—Forlanini's apparatus, modified by Saugman.

ing is inserted into the pleural cavity, and the gas turned on and allowed to run until the required degree of pressure is obtained. From 500 to 2000 c.c. of gas may be introduced and will usually last from two to four months before absorption, when, if necessary, the operation may be repeated.

The use of artificial pneumothorax in **pulmonary tuberculosis** has been so extensive in recent years that we append details as published by Dr. Mary E. Lap-

ham (Amer. Jour. Med. Sci., April, 1912), who had tried it in 15 cases:—  
 "The simplest and most portable apparatus for making nitrogen injections into the pleural cavity is that devised by Forlanini and modified by Saugman by the addition of a manometer (see Fig. 1). The apparatus is mounted upon a board, and consists of two cylinders, *A* and *B*,

each holding about a liter, and connected at the bottom by rubber tubing. Between the two cylinders is a U-shaped water manometer (*M*) 50 to 60 centimeters long. The graduated cylinder *A* contains the nitrogen; the cylinder *B* is filled with an antiseptic solution; *d* is a three-way stop-cock connecting the needle-tube *c* with *A*, or with the manometer *M*. When the needle-tube is connected with *M*, the manometer indicates the intrathoracic pressure, and the respiratory excursions; when connected with *A*, the nitrogen escapes into the pleural cavity. *L* is a glass

pressure to the two manometers, *W* for water, and *Q* for mercury.

"Before attempting to compress a lung, the functional capacity of the other lung and the effect that the increased respiratory demands will have upon it must be carefully estimated. It is not so much the extent as it is the nature and location of the process in the second lung that will determine the advisability of attempting compression. One lung may be safely compressed when a much greater portion of the second lung is in an old, dry, cicatrized condition than if it is involved

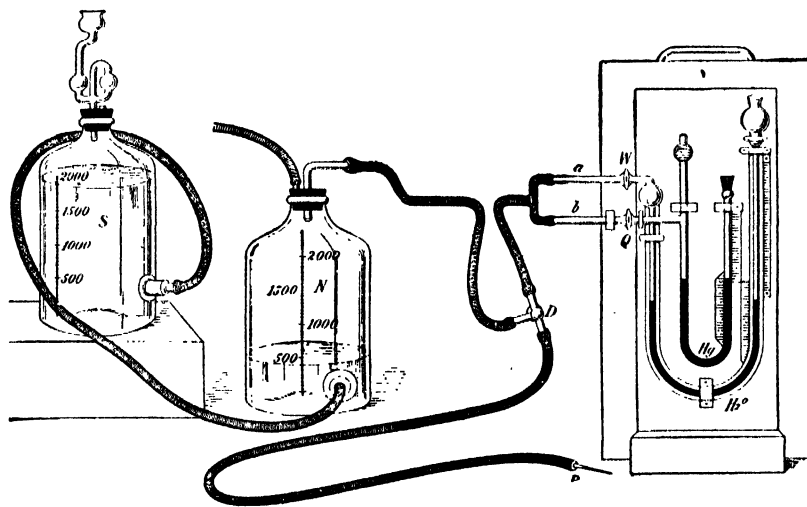


Fig. 2.—Brauer and Spengler's modification of Murphy's apparatus for nitrogen injections.

filter through which the nitrogen must pass both on entering and leaving the cylinder. There is another three-way stopcock, *b*, connected with a bulb. At present this apparatus must be imported.

"Brauer modified Murphy's apparatus by the addition of two manometers, one for water and one for mercury (see Fig. 2). This apparatus may be easily made by using a simple U-shaped water manometer with the two jars. The nitrogen jar *N* is filled with sublimate solution. The water jar *S* is lowered and the nitrogen turned on. The nitrogen is filtered through a glass tube packed with sterile cotton. The supply tube of the nitrogen jar is connected with a three-way stopcock *D*, which will either permit the nitrogen to pass into the pleural cavity through the needle *P* or transmit the interpleural

in a wet, pneumonic process, and apical lesions are not as dangerous as those situated centrally.

"There are two sources of error likely to confuse us in estimating the condition of the second lung. The râles heard over it may be chiefly transmitted from the other lung and entirely disappear as soon as the latter is compressed. On the other hand, deep, central lesions, quite unsuspected at the beginning, may be so aggravated by the increased functional activity of the lung that it will be unwise to persist in the treatment.

"The technique of making nitrogen injections into the pleural cavity is as follows: Choose a spot for making the injection over an area where the breath sounds and resonance are best, in as wide an intercostal space as possible, avoiding

the heart, the diaphragm, and the thicker muscles. Forlanini's method is to place the patient so that the selected site for injection comes uppermost, and arrange the arm so as to widen the intercostal space. Disinfect the skin with tincture of iodine and freeze with ethyl chloride. A fine hypodermoclysis needle may then be thrust through the chest wall until the pleura is felt to yield. Connect the needle with the manometer. If there are no excursions the needle is plugged or is in the lung or a blood-vessel. If for any reason the fine needle is not satisfactory, Murphy advises making a small incision just large enough to admit a medium-sized aspirating needle with a slightly blunted point. As the pleura is felt to yield, air will be sucked through the head of the

action is good, larger quantities at longer intervals may be given. If the heart is weak the pressure should be kept as low as possible and the injections given just often enough to maintain the standard desired. It may not be advisable to raise the pressure much until the heart is found to be equal to the task. When the patient is not incommoded by the pressure, 7 or 8 centimeters will not be too much. Each case is a law unto itself and the proper standard of pressure must be determined for each individual, and then maintained by giving the proper quantity at the right time (see Fig. 3).

"The size and situation of the lung and the degree of compression is best shown by the X-rays. Failing this, the character of the breath sounds indicate the density

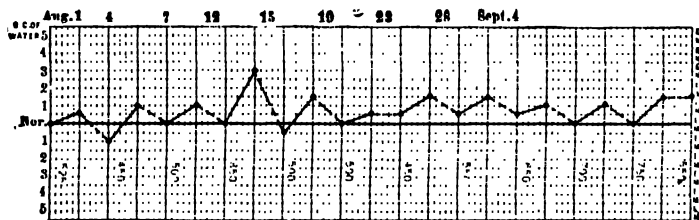


Fig. 3.—Typical curve of pressure within the pleural cavity following nitrogen injections.

needle if there are no adhesions. If this sound is not heard the needle is either stopped up or is in the lung. The needle is then connected with the manometer, and if there are no excursions a new attempt must be made. The safest and most reliable method is that of Brauer, who makes an incision sufficiently long to afford a good inspection of the pleural surface after the tissues are retracted. If the pleura is glistening and smooth, and the motions of the lung are visible, he punctures the pleura with a blunt needle, carrying a fine catheter with which the pleural layers may be explored. When satisfied as to the existence of the pleural cavity, the needle is connected with the manometer. After the nitrogen has been injected, the incision must be closed by carefully suturing each layer of tissues. The after-fillings are made by using a fine needle without an incision.

"The quantity and the frequency of the injections vary with each case. When there are no adhesions and the heart

of the lung, and the area of resonance the extent of the pneumothorax. As the lung becomes compressed, the râles and breath sounds give place to metallic breathing and, finally, to a sharp, metallic clinking, or the sound of a drop falling into a metallic space. When the lung is held out by adhesions, the breath sounds and râles persist over these areas, and metallic conditions are not induced. Bulging over the previously shrunken side is frequently seen, and the difference in motility plainly felt.

"When the pleural layers are held together by bands or adhesions, the clinical course of the treatment is altered, and the technique greatly increased in difficulty, so that we encounter all degrees of failure, from inability to produce a pneumothorax, to inability to compress the lung after it is produced. The dangers attending the method are also increased. Failure of the manometer to show typical respiratory excursions may be due to the inability of the pleural layers to suffi-

ciently separate because of adhesions too near the point of puncture. A little nitrogen may aid in separating the pleural layers and produce perfect respiratory excursions. This is tempting, but dangerous, because without the manometer we have no idea where the point of the needle may be. If we do not have the respiratory excursions to guide us, we are unable to know whether the point of the needle is in the lung, or in a blood-vessel, or whether the needle is simply stopped up. If the pleuræ are adherent they are pierced as one and the needle goes on into the lung. In all probability a fine needle will not injure the lung unless it is moved about sufficiently carelessly to tear the lung tissue. If a large needle is used and the stiletto vigorously employed to ascertain the reason of the obstruction, the lung tissue may be considerably injured and death result from the formation of an abscess. If the wall of a pulmonary vessel is torn, air may be sucked in from the lung, or nitrogen may enter. The point of the needle may be in a blood-vessel, and the nitrogen enter the circulation directly. There is always the danger of embolism whenever a filling is made. Careful technique avoids the introduction of the nitrogen into the circulation, but there are two other theoretical dangers to be considered. It is quite possible that an angiomatous condition of the pleural vessels will cause the needle to tear one of the thin vessel walls without the needle becoming obstructed. Then as the nitrogen is injected it may be forced into the torn vessel. If there are clots in the pleural or pulmonary vessels, the pressure resulting from the filling may expel one into the circulation and thence to the brain. The cerebral phenomena of embolism are loss of consciousness, rolling of the eyeballs upward, contraction of the pupils or dilatation, loss of pupillary reflex, conjugate deviation, extension convulsions, trismus, instantaneous cessation of the circulation and respiration, or prolonged failure.

"Very different are the phenomena due to insult to the pleura or the pneumogastric nerve, known as pleural reflexes. These vary from slight collapse or dyspnea to complete aphonia and spasm of the

glottis. They are avoided by the preliminary use of morphine, whisky, by touching the surface of the pleura with cocaine, and by not using nitrogen below the body temperature. Insult to the pneumogastric nerves may cause paralysis of coughing and speech. A peculiar source or difficulty and danger is found in an excessive development of the pleural circulation resulting almost in a neoplastic overgrowth. Under such circumstances it is difficult to introduce the needle into the pleural cavity without the needle becoming filled with blood, and, even after a pleural cavity of some size has been created, we may fail in the attempt to find it.

"If too much nitrogen is introduced under too high a pressure, the nitrogen may escape back through the track of entry and appear subcutaneously as an emphysema, or it may infiltrate beneath a muscle and lift it up. Instead of leaking out, the nitrogen may produce bulging of the unsupported anterior and posterior portions of the pleura with subsequent escape into the mediastinum, forming deep emphysemas, which crowd up into the neck or press against the heart, causing alarm and distress to the patient."

EDITORS.

Seventeen cases of **pulmonary tuberculosis** treated by artificial pneumothorax. There was a manifest improvement, and in many cases an arrest of the pathological process in caseous pneumonia and rapid phthisis, both clinical forms of pulmonary tuberculosis, in which evolution is quickly fatal and scarcely amenable to former modes of treatment. The operation, however, is not devoid of danger, for in the 17 cases reported there were 3 cases in which subcutaneous emphysema occurred, in 2 cases mediastinal emphysema, in 1 case unilateral convulsions on the left side, and in 1 case immediate coma, with convulsive seizures and death in thirty-seven hours. Piéry (Lyon médical, March 3 and 10, 1912).

Ten cases of **pulmonary tuberculosis** treated by injection of nitrogen into the pleura. Two cases, in

which the treatment appeared to have been successful, were lost sight of. One patient died suddenly while receiving a second injection. Of the remaining 7 cases, the temperature descended to normal in 4, in 1 remained stationary, and in 2 remained at normal; the weight increased in 3 cases, diminished in 2, and remained stationary in 2; expectoration diminished in 5 cases, was uninfluenced in 1, and entirely ceased in 1. Sillig (*Revue de la Suisse Romande*, March, 1912).

The chief dangers are: Pleural reflex, *i.e.*, shock, or even sudden death due to tampering with the pleura. Though this disaster is fortunately extremely rare, yet it may occur, just as it may when one taps a chest for pleurisy, or washes out an empyema cavity.

Gas embolism, from the injection of gas into a vein, instead of into the pleural cavity.

Asphyxia.

Infection, with the production of a pyopneumothorax.

Of the minor complications, faintness during the gas injection, or shortly afterward, is not uncommon. Dyspnea for a few hours is the rule. It causes little discomfort. Slight temporary dysphagia has been recorded. Pleural effusion occurs during the course of treatment in 30 per cent. of all cases. One need rarely interfere, but may aspirate and replace by gas if it is causing any unpleasant subjective sensations. Surgical emphysema, when it occurs, subsides without treatment. It may be prevented by strapping a pad over the site of puncture. Hubert Chitty (*Bristol Medico-chir. Jour.*, June, 1912).

Series of 28 cases of **pulmonary tuberculosis** treated by artificial pneumothorax; all but 3 were advanced cases which had already failed to respond to other measures. A distinct relief of symptoms was the immediate result in practically all. The tuberculous process was arrested in at least 6 under continued observa-

tion; in 2 there was cessation of all activity in both lungs. The writers advise repeated injections of nitrogen, as complete lung compression is thus more nearly attained, and the partial mobilization permitted by absorption of the gas is prevented by its early renewal. No accidents, or deaths referable in any way to the treatment, occurred. Robinson and Floyd (*Archives of Internal Med.* April, 1912).

Artificial pneumothorax is *indicated* in moderately or far advanced cases of **pulmonary tuberculosis** in which ordinary measures are not followed by improvement; in earlier cases in which improvement fails because of mixed infection, low recuperative power, or where condition is stationary or progress very slow; in all rapidly progressing cases; for all patients of the moderately or far advanced types who are discontented and ask for the operation; in uncontrollable hemorrhage or chronic sanguineous expectoration.

It is *contraindicated* in extensive involvement of both lungs; where extensive cavitation of affected lung gives rise to the danger of the needle entering a cavity; by dry pleurisy or pleurisy with effusion; by myocarditis; other serious cardiac complications, or serious renal complications; any case so complicated by other organic disease that recovery is impossible; when patient is too apprehensive and strongly objects to operation.

Various *accidents* liable to occur: air embolisms; cardiac or pleuritic shock causing failure of respiration, spasm of the glottis, aphonia, and inability to cough; injury of blood-vessel or nerve causing hemorrhage or neuritis; pleurisy with effusion; emphysema; pneumonia in opposite lung; distress manifested in anxiety, intense dyspnea, or cardiac pains, and due to the expansion of the nitrogen injected at room temperature (avoided by passing the nitrogen through a coil of metal tubing suspended over an alcohol lamp—if oxygen is used,



the flame should be extinguished before passing the oxygen through, to avoid explosion). S. A. Knopf (*N. Y. Med. Jour.*, Nov. 22, 1912).

Trial of artificial pneumothorax is advised in all one-sided cases where no improvement has been shown, and in which inflation is possible (adhesions not too extensive). If improvement follows, the writers advise continuance, if not to abandon it. F. Fehleisen and M. Rothschild (*Calif. State Med. Jour.*, Sept., 1913).

Artificial pneumothorax not to be abandoned if lung is lacerated by needle (pleuro-pulmonary fistula) as this complication is benign. L. Bard Semaine méd., July 16, 1913).

The more recent development of the question seems to confirm the value of artificial pneumothorax in appropriate cases, *i.e.*, particularly those in which adhesions do not exist to a sufficient degree to prevent sufficient collapse.

The ultimate results of artificial pneumothorax in **pulmonary tuberculosis** in 104 cases divided into 2 series—1 in which treatment has been begun in May, 1912, and the other in August, 1914, are given by the writer. Of these cases 75 were eliminated as inoperable; incidentally they showed that almost 1 case out of 4 has such extensive adhesion that operation is impossible. This left 79 cases that allowed of sufficient collapse to produce therapeutic effects. Of the 79, 35 are dead, 2 were apparently made worse; 18 were improved, and 21 were discharged and treatment stopped as being symptomatically cured. Of the 18 marked "improved" 12 are still under treatment. Of the 21 patients discharged as symptom-free, 19 were third stage, 2 second stage cases, 17 progressive and 4 stationary. The sputum was positive in all. All were febrile cases and all had tried the usual rest cure and climate treatment. The majority were sanatorium cases and all had failed. These patients have now been without pneumothorax treatment as follows: 2 over 3 years; 4 over 2 years; 5 over

1½ years; 6 over 1 year, and 4 over 6 months or over. Two have relapsed and died. Of the remaining 19, 15 are well and working, and 3 others were ready for employment. The writer advises small injections of gas, never exceeding 500 c.c., and as a rule from 250 to 350 c.c. Shoettle (*Jour. Amer. Med. Assoc.*, lxxvii, 1268, 1916).

Since November, 1915, the writer treated 63 cases by pneumothorax. All cases have been classified advanced. He found results undoubtedly encouraging. In 23 cases nothing could be done on account of adhesions. In 21 the results were satisfactory: temperature and pulse became normal, cough and expectoration practically ceased, while tubercle bacilli could not be found in most cases. In 9 cases the results are uncertain; in 10 cases the results were not good. J. Crockett (*Glasgow Med. Jour.*, lxxxviii, 66, 1917).

Out of 30 cases the writer obtained complete success in 7 cases; stopped hemorrhage in 3; beneficial in 2; prolonged life for an appreciable period in 4; and failed in 14. The failures were due in 10 cases to the presence of adhesions which constitute the great impediment to the beginning and the completion of the procedure. P. H. Ringer (*Amer. Jour. Med. Sci.*, Sept., 1917).

Partial collapse of a tuberculous lung tends to give rest to any consolidated portion, and thereby to reduce autoinoculation. The changes which take place as a result of the absorption of gas tend to reduce the amount of strain in the diseased parts when this strain is compared with that which existed before collapse. A single operation for collapse is therefore likely to be followed by good results. A moderate degree of collapse does not materially interfere with respiration provided it allows sufficient normal tissue to function. Both lungs can be treated at one and the same time. W. P. Morgan (*Quarterly Jour. of Med.*, Oct., 1917).

The method is chiefly applicable to moderately advanced, or advanced chronic cases, with or without acute exacerbations, but *not* to florid, acute cases, nor to incipient ones, unless these show an acute waking up. As to the duration of the treatment, after 1 year we should always consider the advisability of removing the gas and allowing the lung to re-expand. Many cases are kept collapsed too long. The procedure may at times be useful in cases of abscess of the lung, and in hemorrhage, if we can be sure of the lung from which the blood comes, it is one of the writer's most valuable measures, granted no adhesions exist. The procedure is unquestionably very dangerous if carried out carelessly, or without the constant use of the manometer, but in careful hands the percentage of danger should be very small, and while the chief danger arises while giving the preliminary injection, air embolism and other dangerous complications can occur during the course of reinjections. Forlanini's advice that small amounts of gas be injected slowly and under low pressure should never be forgotten now in hemorrhage cases. Minor (*Amer. Rev. of Tuberculosis*, Nov., 1917).

When the hemoptysis is extensive, the hemorrhage issuing from an actual tear in some vessel in the lung, prompt resort to artificial pneumothorax may save the patient. After locating the injured vessel by the localized pain, gurgling sounds, râles at the base, etc. The needle is introduced in the third or fourth intercostal space, between the mammillary and anterior axillary lines. From 800 to 1000 c.c. of nitrogen or oxygen or air are introduced, and more is introduced every 4 or 5 days to maintain the compression on the lung. The hemoptysis is usually arrested at once, only rarely is a second intervention of the kind needed in 24 or 48 hours. The use of the manometer has reduced to zero the danger from the procedure. G. Cicconardi (*Riforma Medica*, Feb. 22, 1919).

**Thoracotomy.**—Thoracotomy may consist in a single incision between the ribs, or an incision with the removal of a segment of a rib, or of a much more extensive operation in which the most of the ribs are removed, or in which they are simply divided and an osteoplastic flap made.

**Thoracotomy with resection of a segment of rib** is resorted to when drainage of the pleura is to be established, as in **empyema**, and is much to be preferred to the simple incision between the ribs. Local or general anesthesia may be used. The patient may be placed on the sound side, provided it does not embarrass respiration or circulation. In many patients who have been lying on the affected side for weeks it will not do to place them on the sound side, and a compromise in the way of a dorsolateral position on the sound side is as much as can be borne. The site selected is the same as for aspiration. The incision may be made over and down to the sixth rib, dividing its periosteum. The soft tissues, including the periosteum, are then carefully separated from the rib for a space of about 3 c.c., being careful not to wound the vessels and nerve in the groove on the under border of the rib. The cleared segment of rib is then removed with bone-cutting forceps, and the pleural cavity is opened by an incision through the soft tissues. The finger is inserted, and as far as possible an examination is made as to the condition of the pleura and lung and the size of the abscess cavity, after which a pair of good-sized rubber tubes should be inserted for drainage, and, perhaps, later on, irrigation. Care should be taken to prevent any possibility of the tubes

slipping completely into the pleural cavity, perhaps best done by transfixing the tubes with a large safety pin to which long tapes are attached. Irrigation should not be used until later, and then cautiously until the patient's tolerance is ascertained. As the discharge diminishes and shows a tendency to cease, the tubes are removed and the opening is permitted to close.

**Thoracoplasty.**—In old cases of pleurisy the pleura becomes enormously thickened, binding down the lung and preventing its expansion and the obliteration of the abscess cavity formed by the pleural cavity.

Several operations have also been resorted to in order to relieve these conditions:—

(a) **Decortication of the Lung.**—This is G. R. Fowler's operation, also called Delorme's operation, and in essence consists in stripping the fibrous covering from the lung. In order to expose the lung it is best to make a large osteoplastic flap, by a vertical incision dividing the soft parts near the sternum, then the cartilages at their junction with the third, fourth, and fifth ribs; the soft parts in the third and fifth intercostal spaces are then divided for 4 or 5 inches back and the flap thus made raised up, breaking or cutting the ribs externally, and making a hinge upon which the flap is turned back, exposing the pleural cavity. The lung is found contracted into a small mass occupying the upper part of the pleural cavity. The thick membrane covering it and holding it down is carefully incised and stripped off as far as it can be safely done and cut off with scissors. This is continued until the entire lung is relieved, if possible. In favor-

able cases the lung swells out as soon as the binding tissue is removed. If the operation cannot be done without serious damage to the lung-tissue it must be abandoned. The flap of chest wall is finally restored to its place and fixed by sutures, with or without drainage, as may be required.

Case of a woman 57 years of age in whom **empyema** followed a **stab wound**. Low thoracotomy with rib resection posterior to the midaxillary line, and daily irrigations with hydrogen-peroxide solution, proving ineffective in arresting the flow of pus, lung decortication was performed three and a half months after the beginning of the pleural inflammation. An injection of bismuth had revealed the presence of a cavity only of moderate size, but at operation the pleura covering the lung was found several centimeters thick. As soon as this shell had been removed, the lung expanded and even prolapsed from the wound, thus showing that its elasticity had remained unaffected. The writers review the experiences of Dowd, Ferguson, and Lund with this operation, and believe that its dangers and difficulties have been greatly exaggerated. Picqué and Delorme (*Bull. de l'Acad. de Méd.*, March 26, 1912).

(b) **Estlander's Operation.**—The object of this operation is obliteration of the abscess (pleural) cavity by causing collapse of the chest wall in order to bring the abscess walls in contact with one another. This is done by removal of as many ribs as may be necessary. The ribs may be exposed by making a large C-shaped flap of skin or by horizontal incisions in the intercostal spaces, through each of which two ribs can be removed. It is advisable to remove from 2 to 5 inches of five or six ribs—subperiosteally, depending on the size of the abscess cavity. The pleural

cavity should be curetted or Fowler's operation done at the same time. The chest wall is then held in contact with the lung by means of compresses and bandages.

(c) **Schede's Operation.**—This is the most radical of all the methods of thoracoplasty, and consists in removing the entire chest wall except the skin and fascia. An incision is made from the cartilage of the second rib in front downward along the cartilages to the ninth or tenth rib, backward along this rib to its angle, then upward along the vertebral border of the scapula to the second rib. This flap, consisting of skin, superficial muscles, scapula and its muscles, is raised and the bleeding arrested. The intercostal vessels should be secured beyond the lines of incision before proceeding with the next step, which consists in cutting away with bone forceps and strong scissors the ribs from their costal cartilages nearly to their tubercles, along with the intercostal muscles, fascia, and parietal pleura. The visceral pleura is curetted or decorticated and the large flap placed in position and secured by means of sutures, after which compresses, dressings, and bandages are applied to keep the flap in contact with the lung. This is a very severe operation and is followed by great deformity.

Sauerbruch employed the following method in 35 cases of thoracoplasty: Small doses of morphine or of pantopton were given one hour before the operation. A 0.5 per cent. novocaine solution with the addition of suprarenalin was employed, the solution being made freshly for each operation. According to the extent of the operation, from 10 to 200 c.c. (2½ drams to 6½ ounces) were necessary. The line of the intended incision

was first injected subcutaneously. From this anesthetic line the deeper tissues, chiefly the nerves, were injected. The needle was directed from below and inward, upward, and outward against the rib lying over the point of injection in the region of the angle of the rib. When the needle scraped the bone, 1 to 2 c.c. (16 to 32 minims) were injected. Then feeling for the lower border of the rib, 5 to 8 c.c. (80 to 130 minims) were deposited. At the costal angle the intercostal nerve passes from the middle of the intercostal space upward to the lower border of the rib above. The intercostal veins are already in the groove under the rib above. The injection is made for each rib to be resected. The first intercostal nerve under the first rib is injected successfully in thin patients, but less so in stout patients. For the axillary incision a large injection needle is passed as far as possible posteriorly along the convex border of the rib with continuous injection. In 20 out of the 35 operations, in which 4 to 8 ribs were resected, no chloroform was necessary. In the others a few drops were necessary to induce a partial, light narcosis. No accidents, such as penetration of large vessels, the pleura, or lungs, were observed. Schumacher (*Amer. Jour. Med. Sci., from Zentralbl. f. Chir., Bd. xxxix, S. 252, 1912*).

**Pneumotomy.**—This operation consists in cutting into the lung for any purpose, as to remove a **foreign body** or to drain an **abscess**, ordinary, **tuberculous**, or **bronchiectatic**. The lung may be exposed by resecting one or two ribs, or by a flap of the chest wall and the foreign body, or abscess may be located by means of an exploring needle. The lung-tissue may be divided by a blunt instrument like the surgeon's finger, the thermocautery, or a knife. It may be advisable before entering the lung-tissue to

cause adhesion between the pleural layers by stitching them together and waiting a week or ten days before going farther.

Case of a boy aged 12 years who five weeks previously had swallowed a large blackheaded pin. No symptoms appeared for a week, when cough began; a week later the sputum was blood-stained. Radioscopic examination showed the pin to be lying in the left lung, the point toward the trachea. A curved incision was made over the left chest, six inches of the left eighth rib were incised, and air was cautiously allowed to enter the left pleura through a small puncture. The lung, which was collapsed, was held firmly; a small incision was made over the head of the pin, through which it was withdrawn with a pair of sinus forceps. There was no hemorrhage, but abscess formation had already begun. No suture was put into the small wound in the lung. No sup-puration of the pleura took place, and the patient was perfectly well twelve days after the operation. The great value of radiography is shown by the fact that foreign bodies almost invariably enter the right bronchus, instead of the left, as in this case. Russell and Fox (*Lancet*, Sept. 9, 1905).

**Pneumectomy.**—The removal of a portion of a lung may be indicated on account of malignant disease, as **cancer, tuberculosis, for gangrene, or for severe injuries.** Murphy and others have shown that two-thirds or more of one lung of a dog can be removed without causing death, but, as remarked by Brewer, "the removal of a divided or injured portion of lung in the human subject has thus far been attended by a high mortality." Exposure is best obtained by the osteoplastic flap. The portion of lung to be removed is drawn out, transfixed, and ligated with chromic

catgut and cut off, or Green's method may be used. He passes a ligature by means of a needle beneath the pleura so as to encircle the lung beyond the point to be divided, draws this tight and ties it, removes the portion of lung, and then unites the pleural edges of the stump by means of sutures.

Despite the few successful cases reported, lung excision will eventually justify its existence as an operative risk. The dangers are: operative injury to important nerves, shock, overflow or inhalation of the purulent secretions into the sound lung, with resulting transplantation of the infection. The duration of the disease and the resistance of the patient will affect the prognosis greatly. Since the complete operation is a formidable one in patients with reduced resistance, it should be divided into two or more stages. If sputum is to be contended with, as in bronchiectasis, the first stage includes resection of the ribs, opening of the pleura, and either a pneumotomy for drainage, or ligation of the lobe. At another stage the adhesions are separated, and if this causes extensive lacerations the infected lobe is packed off and removed a week later. If the lacerations are slight, the lung may be removed at the second operation. If sputum is not an obstacle, two stages are best, rib resection, thoracotomy, and freeing of adhesions at one stage, and amputation at a later operation. Endotracheal insufflation of gas and oxygen is better in thoracic surgery than ether. A semisitting posture during operation is necessary. Robinson (*Annals of Surg.*, April, 1912).

History of a patient who received a bullet wound in the right thoracic cavity. A pulmonary fistula resulted, followed by a series of empyemata, which did not give way to drainage or various forms of irrigation. After an extensive thoracotomy, the lung was freed from all

adhesions, the fibrous layers adherent to the lungs peeled off and then the pulmonary parenchyma surrounding the fistula resected. A large cavity resulted which was closed by sutures. Later a cutaneous flap operation was done to close the thoracic wound. The patient made a good recovery. The writer then studied the distribution of the bronchial tubes, since in resection of the lung, the operation must depend upon their anatomic arrangement. This is as follows: The bronchi form cones with the apex directed towards the hilum; the base is oval in shape, the great axis being anteroposterior, but the lesser axis vertical.

As to operative indications, the writer mentions pulmonary fistula, especially when the pleural cavity is filled with adhesions. Resection is less to be recommended in cases of neoplasms, tuberculosis, extensive bronchial dilatation, and multiple pulmonary abscesses. Lastly, he insists upon the advantages derived from pulmonary amputation which ensues after removal of the atelectatic tissue and fibrous layers which fill the pleural cavity. M. Zondek (*Berl. klin. Woch.*, Apr. 8, 1918).

**Paracentesis Cordis.**—Aspiration of one of the chambers of the heart in order to relieve it of dangerous pressure is said to have been done. With care and the use of a small aspirating needle there would seem to be little danger in the operation. The writer once aspirated the left side of the heart (probably the ventricle) with a hypodermic syringe and needle, withdrawing 25 minims of bright-red blood without harm to the patient.

The chamber recommended for aspiration is the right auricle, and the operation is performed by thrusting a long aspirating needle into the third right intercostal space close to the edge of the sternum and passing it

directly backward from 2 to 3½ inches, depending on the thickness of the chest wall, until dark blood flows freely.

There can be no doubt that aspiration of either ventricle would be safer than that of the auricles so far as the danger from hemorrhage is concerned, as the ventricular walls are so thick that the small wound produced by the needle would close more or less completely on its withdrawal. Such a wound in a thin-walled auricle might ooze for a while and form a clot in the pericardium which might give trouble. A needle passed directly backward in the fourth left interspace close to the sternum would be almost certain to enter the right ventricle. To enter the left ventricle the needle would have to be inserted in the same interspace, but about 2 inches to the left of the sternum, and carried backward and inward. A more certain way would be to insert the needle as if to aspirate the right ventricle, and pass it through the right ventricle and interventricular septum into the left ventricle, the entrance into which would be indicated by a flow of bright-red blood.

**Paracentesis Pericardii.**—This operation is indicated when the accumulation of serous fluid or blood in the pericardium seriously embarrasses the heart and no necessity exists for a more radical operation. The needle may be inserted in the fifth left interspace close to the sternum or 2 inches to its left—to avoid the internal mammary vessels—or the needle may be passed upward through the triangle formed by the ensiform cartilage and left costal cartilages. The heart is less apt to be wounded if the pericardial sac is opened near

the lowest point, as it is here the fluid accumulates and pushes the heart upward and forward.

The best place for aspirating in case of extensive exudates, and perhaps even in smaller ones, is the lower part of the pericardium, entering from the left costoxiphoid space. This point is preferred by Shattuck, Fitz, and Osler, and it is becoming more and more favored for radical operations.

If puncture is negative in the location first chosen it should be repeated with a change of position of the patient, and if still negative in another place. In many cases puncture is negative in one place, positive in another, or negative with the patient recumbent, positive when sitting up or leaning forward.

When found, the fluid should be removed as completely as possible. Sometimes removal of a small quantity for examination has seemed to stimulate absorption, as we see in pleurisy, but complete or repeated aspiration is often necessary. A case of Döbert's is instructive in connection with some of the statements just made. At intervals of four days he obtained 130, 150, and 200 c.c. ( $\frac{4}{8}$ , 5, and  $6\frac{3}{4}$  ounces) of fluid; still later, 500 (1 pint). In another case he withdrew 12 c.c. (195 minims) on the right side; later, 400 c.c. ( $13\frac{1}{2}$  ounces) on the left side, none on the right side while lying down, but 300 c.c. (10 ounces) on raising the patient. Dock (Physician and Surgeon, June, 1907).

Three cases illustrating the good results of puncture of the pericardium from the back. The writer was driven to this in the first case by the **extreme dilatation of the heart following acute rheumatism**, and by the excitement of the patient, a nervous girl of 16. He punctured through the eighth interspace from the rear and siphoned out 350 c.c. (12 ounces) of effusion. Six months later, except for slight modification of the first sound at the apex, the

heart and circulation were normal. Convalescence from the pericarditis was retarded by chorea with stupor and hallucinations, all subsiding in three weeks. In the second case, a man of 50 was relieved by puncture from the rear; the writer's only trocar was short and wide, and he did not like to introduce it too close to the heart. In the third case there was so much edema in the skin of the left chest that he did not dare to puncture through its unknown depth. He cites his father's case in which a man of 32, otherwise healthy, would not allow puncture and died suddenly before he could be persuaded to permit it. Such cases probably are more frequent than generally supposed; puncture from the rear would rob the procedure of much of its terror for the patient. Such effusions are mainly encountered in young persons after acute rheumatism, and the heart is generally much dilated. Curschmann (Therap. Monats., May, 1912).

#### **EMPHYEMA OF THE PERICARDIUM — PYOPERICARDIUM —**

should be treated by free opening and drainage of the sac. This is best done by resecting a portion of the fourth or fifth left costal cartilage, ligating the mammary artery if necessary, finding the pericardium, and carefully opening it so as not to wound the heart or infect the pleural cavity. Drainage should be provided, usually by means of gauze, and the surrounding tissues protected from infection, if necessary, by sewing the edges of the pericardium to the superficial structures. Irrigation may be used later on. Porter's statistics some years ago of 51 cases of pyopericardium treated by incision and drainage gave 20 recoveries and 31 deaths.

**Pericardiectomy.**—Having observed that a number of cases of congenital abscess of the pericardium had been reported in which there

were no symptoms during life, Parla-vecchio made experiments on 10 dogs in order to determine the practicability of its performance as a therapeutic measure. He concludes that it is an operation comparable with splenectomy or partial thyroidectomy, and that it offers good prospects of success in **malignant disease** or in **chronic pericarditis**. One phrenic nerve can be divided with impunity, but not both. Some of the dogs were in good health five or six months after operation.

Removal of the pericardium should be resorted to only as a last resort, but under these conditions it has good prospects of success. Broad resection of the pericardium may be considered in **cancer** of the adjoining organs or in **chronic pericarditis** resisting conservative measures. It would leave a defect which might favor infection of the pleura, but pleurisy is much easier to cure than pericarditis, and it is the less of two evils. The Rydygier technique gives ample access. Removal of the left phrenic nerve does not impair the functions of the diaphragm, while its retention might result in dangerous adhesion of the nerve to the heart. The technique should be dominated by the necessity of avoiding injury of the auricles and large vessels. The surgeon should refrain from touching the right wall of the pericardium, for fear of injuring the phrenic nerve or the other pleura, which would be liable to cause paralysis of the diaphragm or bilateral pneumothorax. In none of his dogs were the adhesions after pericardiectomy very serious. The fewest adhesions were found in dogs with more extensive resection. Parlavecchio (Policlinico, Aug., 1908).

#### **MASSAGE OF THE HEART.—**

Many experiments have been made on the hearts of the lower animals in order to restore pulsation after death,

and by pumping fluid through the coronary arteries the heart has been made to pulsate eighteen to twenty hours after death, and even some hours after complete separation from the body. But return of heart pulsation does not always mean return of life in the patient. Life has been restored in the dog by heart massage combined with artificial respiration fifteen minutes after the heart has ceased to beat (Batelli) and in man after twenty-five minutes (Wayne Babcock). Heart massage, usually by the abdominal method, has been practised now a great many times. One of us has practised it about half a dozen times—including both methods, thoracic and abdominal—with varying success. It is impossible to say just how long after cessation of the heart's action heart massage may be able to revive it, but certainly after five or ten, and, perhaps, after fifteen or twenty, minutes—or longer.

**Thoracic heart massage** is but seldom done—except when it becomes necessary during an intrathoracic operation—as the chest must be opened by one of the methods described under Wounds of the Heart. The heart is then grasped with the hand outside of the pericardium, or, if open, the fingers should be introduced into the pericardium, and rhythmically and firmly squeezed about once a second. At the same time artificial respiration should be kept up. These should be kept up for at least fifteen minutes.

**Abdominal heart massage** is made through the abdominal cavity, the fingers grasping the heart through the diaphragm or pushing it against the chest wall in order to compress



it, as already described. Often the necessity arises during an operation in which the abdomen is open; otherwise, the abdomen should be opened in the median line above the navel; the hand is introduced, and the heart compressed through the diaphragm by taking hold and squeezing it if possible; otherwise, by pressing it against the chest wall or against the other hand pressed against the chest wall.

Case of a young man who died while being operated upon for tuberculous peritonitis under **chloroform anesthesia**. His heart had stopped beating forty-five minutes, his respirations had ceased, and his pupils were widely dilated. The writer opened the pericardium, massaged the heart, and applied hot compresses to it while artificial respiration was being performed. In half an hour the heart was beating strongly and regularly, and life was again resumed, the patient living for twenty-seven hours, when he died in collapse. Paul Sick (Zentralbl. f. Chir., Sept. 5, 1903).

Case of a man who had received a gash across the chest with a razor. The patient was in shock when first seen, and was given 20 ounces (600 c.c.) of saline solution by hypodermoclysis and injections of strychnine and nitroglycerin. In a short time some improvement was noted, and an attempt at repair was made under partial anesthetization with ether. The wound began at the junction of the outer and middle third of the clavicle on the left side, and extended downward and to the right to a point four inches below the right nipple. The muscles were entirely divided, as was the left third rib at its cartilaginous junction, while the second and fourth ribs were almost divided. Suture of the wound from either end toward the center was proceeded with, and while the opening at the center was being packed with gauze

it was noted that the patient was in a bad state. He was given cardiac stimulants by the subcutis, and artificial respiration was started, but to no avail, and the man had apparently died. The index finger of the operator was passed in through the wound and the heart felt to be perfectly still. The heart was then seized between the thumb and forefinger and manipulated for forty to sixty seconds, when a slight thrill was felt. Action of the heart was slowly re-established, and soon a pulse was felt. The opening was then packed, and the patient put to bed and given saline solution and stimulants. Recovery was uneventful, and in four weeks the wound was filled with granulations.

The author estimates that the heart had ceased to beat at least two minutes before massage was started. Two months have elapsed since the injury, and the patient is well and expects to go to work soon. Conkling (N. Y. Med. Jour., Sept. 2, 1905).

Case of a woman aged 55 years who was suffering from marked laryngeal obstruction. High tracheotomy was done, but after two or three breaths had been taken the patient apparently died, there being no pulse, and no cardiac sounds were heard on auscultation. A few minutes later the abdomen was opened in the middle line immediately under the xiphoid cartilage, two fingers were inserted, and the heart massaged between the diaphragm and the ribs in front. It was compressed about seventy times a minute for three or four minutes, when it gradually became firm, trembled, and slowly began to beat. A few minutes later, it was beating at the rate of ninety in a minute. All this time artificial respiration was kept up. The patient died about two hours later. At the autopsy there was found a fairly large **cancerous growth in the larynx**. Gray (Lancet, Aug. 19, 1905).

Forty cases of massage of the heart in cases of **apparently sudden**

**death**, including 2 cases of his own, found in literature. In suitable circumstances it is a method of treatment which should commend itself to the practical surgeon. Green (Lancet, Dec. 22, 1906).

Eight recoveries due to heart massage out of 50 reported cases in which it was used. Heart-failure is rarely primary in **chloroform anesthesia**; it is, therefore, essential that respiration be invoked by artificial means in conjunction with heart massage. Artificial respiration alone will not inaugurate heart contractions nor maintain blood-pressure. The best results have been obtained by the subdiaphragmatic method. The most frequent indication for its use is in chloroform narcosis with cessation of respiration and circulation. In other conditions of heart-failure secondary to respiratory failure and not dependent upon organic changes in the heart, the method is applicable. C. S. White (Surg., Gynec., and Obst., Oct., 1909).

In the case of a wounded soldier resuscitated by cardiac massage, the movement of lifting him from the stretcher on to the table appears to have been the deciding factor in the cardiac failure. Sichell (Brit. Med. Jour., Feb. 5, 1916).

Case of heart failure in a boy of 6 years during an operation for the **removal of tonsils and adenoids**, treated by heart massage, with recovery. W. M. Mollison (Lancet, Nov. 25, 1916).

The writer successfully practised massage of the heart through the diaphragm in 2 cases in which it had stopped beating during operation. Artificial respiration was also maintained. E. S. Molyneux (Brit. Med. Jour., Mar. 31, 1917).

The writer makes an abdominal incision 4 inches long in the median line, extending from above the umbilicus well up into the xiphosternal notch. The left costal cartilages are well retracted, bringing the anterior diaphragmatic insertion well into view. A 2-inch incision, beginning 1 inch to the left of the median line

carried outward behind the costal margin, cuts the fibers of the diaphragm near their insertion. A blunt instrument pushed in opens the pleural cavity, and the opening is rapidly dilated with 2 or 3 fingers of the right hand, so that the whole hand can then be passed into the thoracic cavity anterior to the pericardium. The hand is passed upward, the thumb behind the sternum and the fingers embracing the entire organs in the pericardium. The thumb compresses the right auricle and ventricle, and the base of the heart is effectively massaged. T. C. Bost (Indian Med. Gaz., Feb., 1919).

The heart may also be compressed and possibly excited to action, especially in very young persons, by pressure over the fourth and fifth cartilages and ribs on the left side without any cutting operation. Heart massage is resorted to when from various causes the heart ceases to beat, as from **anesthesia**, from **hemorrhage**, **shock**, **asphyxia**, or **pulmonary embolism**. Naturally one hesitates to resort to it until he has tried artificial respiration, unless the chest or abdomen are already open, as during a surgical operation. Some lives have undoubtedly been saved by heart massage, and in cases where artificial respiration and other methods have failed no hesitation should be felt in opening the abdomen and trying long and faithfully heart massage, together with artificial respiration.

[The following case, recently reported by W. Wayne Babcock, of Philadelphia (Monthly Cyclopedia and Medical Bulletin, Dec., 1912), is so instructive that we publish it *in extenso*.—

"Mrs. A. D. C., an obese colored woman of 38 years. Nullipara. Ill seventeen years with pain in the right inguinal region, and had noticed progressive abdominal enlargement for fifteen years. No metrorrhagia. The patient entered the Samaritan Hospital Dec. 5, 1911. The

day following she had  $\frac{1}{2}$  gr. (0.0108 Gm.) of morphine with  $\frac{1}{100}$  gr. (0.0006 Gm.) of scopolamine by hypodermic at 2.45, and also at 3.15 p.m. About 3.52 p.m., as the patient was rapidly becoming stupefied by the narcotic, 5 cg. ( $\frac{1}{2}$  grain) of alcoholized stovaine were injected into the twelfth dorsal interspace. The injection was given in the sitting posture, and, on account of her obesity, there was some delay in placing the patient supine upon the table. About three minutes after the intradural injection a median abdominal incision was made. The blood was very dark, and no pulsating vessels were noticed. On examination, it was found that the patient was not breathing, and that the teeth were clenched tightly and the mucous membrane cyanotic. With some delay and difficulty the teeth were pried apart, the tongue pulled forward, and artificial respiration by rhythmic compression of the thorax attempted. These efforts seemed entirely inefficient, the diaphragm being high, the chest short, thick from fat, the abdomen distended and splinted by the large fibroid tumor present, and the neck short and fat, rendering the upper air passages difficult to manipulate. As the patient was pulseless at the wrist, the hand was introduced through the incision, the abdominal aorta grasped, and found also pulseless. Carrying the hand up to the diaphragm, the heart could be felt, apparently rather large and flabby, but without any contractions. Cardiac massage, instituted through the diaphragm, produced no response. Attempts were again made at artificial respiration, while an assistant endeavored to introduce normal saline solution with adrenalin into a vein of the left arm. After some difficulty it was found that the vein, which was rather collapsed, had not been properly entered, so that the fluid was merely distending the tissues. The assistant was, therefore, directed to try the opposite arm. The patient was now relaxed, the mucous membranes were ashy, the skin was cold, there were no evident reflexes, and the every appearance of death was present. An attempt was made to use oxygen through the mouth. Full doses of caffeine and strychnine were injected subcutaneously,

and, as the efforts at artificial respiration failed to oscillate fibers of cotton fastened in front of the nose and mouth, tracheotomy was rapidly done and a trachea-tube introduced. An effort was then made to inflate the lungs by an intermittent flow of oxygen from the oxygen tank, but the volume of the stream was insufficient. The arms being held above the head, repeated and continued efforts were made to establish respiration by thoracic compression, which was stopped from time to time only long enough to permit the hand to be introduced under the diaphragm, and the heart to be compressed or massaged against the overlying chest wall. Finally, it was observed that the saline solution supposed to be running into the vein of the right arm was dripping from the arm, and in enlarging the incision I found that the vein had been punctured, and that the needle lay alongside the vessel. The needle was properly introduced into the vein and the flow of salt solution and adrenalin continued. For perhaps the fifth or sixth time I again introduced the hand and arm into the abdomen and renewed the intermittent compression of the heart, hoping to force out sufficient blood to enable the adrenalin to enter the chambers. The patient had now been apparently dead about twenty-five minutes. Suddenly the hand, grasping the heart, felt a violent and startling thrill, succeeded by rapidly increasing and more violent cardiac contractions. The pulse reappeared at the wrist, the incisions in the arms and abdomen started to bleed, and the ashy color faded from the mucous membrane. The cardiac movements were so violent that the flow of adrenalized saline was checked. A few minutes later the heart grew weaker, the pulse faded from the wrist, and it was evident that the cardiac action could not continue without efficient respiratory action. The flow of oxygen through the trachea-tube was discontinued, and I applied the end of a soft-rubber drainage-tube against the tracheal opening, and blew violently into the lungs. I was gratified to note that the chest expanded, and that on the removal of the tube the collapsing chest forced a part of the air out. I continued intermittent insufflation and had the flow of the solution

resumed from time to time, as seemed to be required. The pulse now returned and was fairly sustained. An assistant continued the efforts of insufflation. About 4.30 P.M., or about thirty-five minutes after apparent somatic death, the first faint voluntary respiratory movement was observed. Gradually voluntary respiration was resumed. The abdominal incision was closed, and the patient returned to her bed with a temperature of 97°, respiratory rate of 24, and pulse of 112. The patient did not regain consciousness, but winking could be produced by tapping the nose. Some pulmonary edema was evident from the passage of blood and mucus along the trachea-tube. The day following, the temperature reached 102½°. The respiration was more noisy, rapid and labored, and finally reached 50, while the pulse rose to 160. On the second day at 11.10 A.M., or forty-three hours after the operation, the patient died, the rectal temperature being 107½° at the time of death." Ed.]

A new method of cardiac massage. Massage through the thoracic wall as usually practised being time-consuming and requiring the turning back of a flap of the chest, while exposing the patient to the danger of pneumothorax, the writer, to avoid this danger, has suggested a simple method of cardiac massage, using a single finger introduced through a stab wound to the left of the heart. The puncture is made one inch to the left of the sternum in the fourth interspace; the finger instantly pushed through the intercostal space and hooked around the left edge of the heart, which is then intermittently compressed against the overlying sternum. This procedure has brought about resumption of cardiac beats in several cases. W. Wayne Babcock (Monthly Cyclopaedia and Med. Bull., Dec., 1912).

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**CHICKEN-POX.** See VARICELLA.

**CHILBLAIN.** See PERNIO.

**CHIMAPHILA** (or *pipissisewa*) consists of the leaves of *Chimaphila umbellata*, or prince's pine, an evergreen plant of the nat. ord. Ericaceæ, indigenous to the United States, Europe, and Asia. The leaves contain arbutin, tannic acid, and chimaphilin, which is a yellowish crystalline substance.

**PREPARATIONS AND DOSE.**—The fluidextract is semi-official (*fluidextractum chimaphila*, N. F.), and is given in the dose of ½ to 2 drams (2 to 8 Gm.). A decoction, not official, is given in the dose of 1 to 3 ounces (30 to 90 Gm.).

**THERAPEUTIC USES.**—Chimaphila is tonic, astringent, and diuretic, resembling buchu and uva ursi in its action, and is used for the same conditions. It is more powerful, however, than either of the above-named drugs, and stimulates all the excretory organs, but especially the kidneys. It is a good remedy in renal atony, as it invigorates the secreting epithelium of the kidney and tones up the whole genitourinary tract. It is also a good tonic, stimulating the secretions of the stomach and thus promoting appetite and digestion. In chronic nephritis, dropsy, or catarrhal conditions of the genitourinary tract the drug is useful. It has been used externally in the treatment of ulcers, and special alterative qualities have been claimed for it in scrofulous affections.

W.

**CHIRATA** (*chirata*, N. F. IV, and B. P.) is an Indian plant, *Swertia chirata*, or *Chirata ophelia* (nat. ord. Gentianaceæ). The leaves and lighter stems are the portions used in medicine. Chirata resembles gentian in its therapeutic properties, is intensely bitter, and without odor. It contains chiratin and aphelic acid, two amorphous, bitter principles, but is devoid of tannin.

**PREPARATIONS.**—Fluidextract of chirata (*fluidextractum chirata*, N. F. and B. P.). Dose, 10 minims to a dram (0.6 to 4 c.c.). Tincture of chirata (*tinctura chirata*, B. P.), strength 10 per cent. Dose, ½ to 4 drams (2 to 16 Gm.). Infusion of chirata (*infusum chirata*, B. P.). Dose, 1 wineglassful. The powder may be given in the dose of 15 to 30 grains (1 to 2 Gm.).

**THERAPEUTIC USES.**—Chirata is a simple bitter, and, being devoid of tannin, may be given in preparations containing iron. It is a reliable tonic and is useful in **atonic dyspepsia**, chronic **gastric catarrh**, **flatulence**, and **acidity**, and in convalescence from acute diseases. In **hepatic atony** the drug is valuable, as it exerts a distinct influence over the liver functions, and is slightly laxative. W.

**CHLORAL HYDRATE** (*Chloralum Hydratum*; Hydrated Chloral; "Chloral").—This substance, a member of the group of drugs known as hypnotics or soporifics, is chemically hydrated trichloroacetaldehyde [ $\text{CCl}_3\text{-CH}(\text{OH})_2$  or  $\text{CCl}_3\text{CHO} + \text{H}_2\text{O}$ ]. It is a distinct compound from pure chloral, which it is sometimes erroneously called, differing from it in that it contains, in each of its molecules, the elements of an additional molecule of water. True chloral, occurring as a pungent, oily fluid, when placed in contact with water absorbs it and gives rise to the solid substance chloral hydrate or, more precisely, hydrated chloral.

Chloral hydrate is commonly made by saturating absolute alcohol with dry chlorine gas, acetaldehyde being first formed and subsequently three of its hydrogen atoms replaced by chlorine. The product is purified successively by sulphuric acid and lime, and presents itself in the form of colorless, transparent, rhomboidal crystals having a rather penetrating, acrid odor and a sharp, burning taste. Upon exposure to the air, hydrated chloral undergoes gradual volatilization; hence it must be kept in well-closed containers. It melts at  $58^\circ \text{C}$ . and boils at  $97^\circ \text{C}$ . It is extremely soluble in water, 4 parts of chloral hydrate dissolving in 1 part of water

—a 400 per cent. solution. It also dissolves readily in alcohol, ether, chloroform, glycerin, and oils. When triturated with an approximately equal amount of camphor, menthol, phenol, thymol, or antipyrin, chloral hydrate forms a fluid mixture.

Impure preparations of the drug, contaminated with chloral alcoholate, hydrochloric acid, chlorides, etc., are sometimes met with. A fair idea of the purity of a sample may be had by pressing it between two sheets of blotting-paper, when, if it is impure, oily spots will be formed. It should make a neutral solution in water, and, when the solution is acidulated with nitric acid and silver nitrate added, no white precipitate should result. The U. S. Pharmacopœia requires that when chloral hydrate is treated with sulphuric acid and the mixture warmed no blackening shall take place.

For information upon drugs related to chloral, such as chloralformamide, croton chloral, chloretone, and chloralose, the reader is referred to the corresponding separate headings.

**DOSE.**—Hydrated chloral is administered in doses ranging from 5 to 60 grains (0.3 to 4 Gm.), according to the purpose for which it is used. The average dose is officially given as 15 grains (1 Gm.). In infants and children, 1 grain (0.06 Gm.) for every year of age may be safely given.

**MODES OF ADMINISTRATION.**—Chloral hydrate is unsuited for subcutaneous administration, owing to the marked degree of local irritation produced. When given by the mouth it should always be prescribed in a well-diluted solution in order to avoid, in so far as is possible, gastrointestinal irritation. Its unpleasant, burning taste may be partly

disguised by prescribing it in a syrup, elixir, or mucilage, *c.g.*, in the following:—

℞ *Chlorali hydrati* .... gr. c (6.5 Gm.).  
*Mucilaginis acaciæ*,  
*Syrupi aurantii* ... āā f℥iss (45 c.c.).  
*Olei menthæ piper-*  
*itæ* ..... gtt. iij (0.18 c.c.).

M. Sig.: One dessertspoonful in water at night.

Sodium bicarbonate may likewise be included in the prescription with advantage. According to Bresslauer and Joachim, the administration of 15 grains (1 Gm.) of sodium bicarbonate fifteen to thirty minutes before and after the ingestion of chloral hastens its absorption, while the use of the same amount after the awakening promotes elimination of the drug and lessens the after-effects. Hot milk is an excellent vehicle for chloral hydrate; besides diminishing its irritating effect on the mucous membranes, it tends to accelerate the already rather prompt absorption of the drug. Syrup of tolu, elixir of orange, lemonade, syrup of citric acid, and junket are other useful vehicles.

Combination of chloral with bromides is frequently resorted to. For hypnotic purposes the following formula will be found useful:—

℞ *Chlorali hydrati* ..... ℥j (4 Gm.).  
*Potassii vel sodii brom-*  
*idi* ..... ℥iij (12 Gm.).  
*Syrupi aurantii* ..... f℥iss (45 c.c.).  
*Aquæ destillatæ*,  
 q. s. ad ..... f℥iij (90 c.c.).

M. Sig.: One dessertspoonful at a dose, in plenty of water. Not to be repeated more than twice, at hourly intervals.

For the relief of convulsions, in cases where the drug cannot be swallowed, chloral hydrate may be very advantageously given by rectum, in doses of 20, 30, 40, or even 60 grains

(1.3 to 4 Gm.). The menstruum used may be either water alone, starch water, or milk. Richmond gives the drug thus:—

℞ *Chlorali hydrati* ..... ℥ss-j (2-4 Gm.).  
*Titellus ovi* ..... no. j  
*Lactis* ..... f℥iij (90 c.c.).

M. Sig.: Inject by means of a rubber hand syringe.

Chloral suppositories, each containing 5 grains (0.3 Gm.) of chloral hydrate and 10 grains (0.6 Gm.) of cacao butter, cannot be made with heat, as the mixture will not set firmly; they are produced, instead, by compression in molds. Their action is likely to be accompanied with considerable local irritation.

In children Comby administers chloral as follows:—

℞ *Chlorali hydrati* .. gr. viiss (0.5 Gm.).  
*Syrupi aurantii* ... f℥v (20 c.c.).  
*Aquæ destillatæ* .. f℥ij (60 c.c.).

M. Sig.: One teaspoonful every hour (in a child 5 years of age).

(Or,

℞ *Chlorali hydrati* .. gr. viiss (0.5 Gm.).  
*Aquæ bulliatæ* .... f℥iss (45 c.c.).  
*Titellus ovi* ..... no. j.

M. Sig.: Administer as enema.

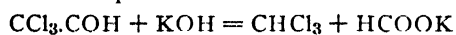
A suppository containing 1½ grains (0.1 Gm.) of chloral hydrate for every year of age might also be used.

**CONTRAINDICATIONS.** — In cases of weak heart action where the presence of fatty changes is considered likely, chloral hydrate should be avoided because of its tendency to produce undue depression of this organ. In other forms of cardiac disease the drug should be used only in small doses, if at all. In passive hyperemia of the brain the result of failure of compensation, chloral is particularly contraindicated (Croftan).

Where the medullary centers are depressed, as well as in serious affections of the lungs, the use of chloral is unwise. In inflammatory diseases of the stomach the irritant properties of the drug are objectionable. Finally, in renal disease chloral is said to irritate the kidneys; caution is therefore required in its employment in these cases.

In general, the first dose of chloral given to any patient should be small, as certain individuals show an idiosyncrasy toward it which may lead to the unexpected appearance of symptoms such as delirium, if a full dose be administered at the outset.

**INCOMPATIBILITIES.** — Hydrated chloral is incompatible with hydroxides of the alkalis, which decompose it with liberation of chloroform and potassium formate:—



It is also incompatible with compounds of lead and mercury, with iodine, potassium iodide, and potassium permanganate. When it is dissolved in alcohol of high percentage, the molecule of water present in hydrated chloral is removed, and the chloral itself combined with alcohol to form an alcoholate  $[\text{CCl}_3\text{CH}(\text{OH})\cdot\text{OC}_2\text{H}_5]$ .

#### PHYSIOLOGICAL ACTION.

**Local.**—Used externally, chloral hydrate is both irritating and anesthetic. The former effect is sufficiently marked to induce redness and even vesication when a concentrated solution of the drug is applied to the unbroken skin. The anesthetic effect is better obtained from more dilute solutions. Subcutaneous injection of the drug causes so much local irritation as to be, for practical purposes, devoid of any value.

Pronounced antiseptic properties are also possessed by chloral hydrate.

**General. Nervous System.**—Hydrated chloral is a powerful sedative to the central nervous system, acting in much the same manner as chloroform save in that its absorption and elimination, as it is ordinarily given, are slower, and the effects correspondingly less violent and more protracted. Small or average doses of the drug act chiefly upon the centers of intellection in the brain, which they so paralyze as to produce sleep. In general, the sensory centers are not nearly so much obtunded by moderate doses of chloral hydrate as is the case with morphine; hence in the presence of pain it is not by any means so efficient as the latter drug. Similarly, where there is great exaggeration of the reflexes, unusual doses of the drug are necessary if sleep is to be induced. Large doses of chloral hydrate cause, in addition to a deepening of the effect already mentioned, with resulting profound sleep, stupor, or actual coma, depression of the motor tracts of the spinal cord, in consequence of which reflex action is greatly diminished or abolished. Toxic doses produce, almost simultaneously, relaxation of the muscles, owing to complete paralysis of the motor nervous mechanism, and general anesthesia, due to an additional effect on the sensory centers. Depression of the medulla, including the respiratory and vasomotor centers, is also caused by large doses of hydrated chloral.

Fatal doses produce death generally by paralyzing the centers of respiration, asphyxia resulting.

In the lower animals chloral allays pain to a greater extent than in man.

In veterinary practice it is used as a specific for colic.

*Circulation.*—Small or average doses of hydrated chloral exert little or no depressing effect on the circulation except in certain individuals specially predisposed through cardiovascular disease or idiosyncrasy. Larger doses, however, tend to depress markedly both the heart and the muscular tissue in the vascular walls. The heart action being both slowed and weakened and the tonicity of the vessels decreased, a considerable reduction of blood-pressure takes place. Poisonous doses induce, like chloroform, dilatation of the cardiac walls, accompanied by collapse and cyanosis, and sometimes followed by arrest in diastole. It is generally conceded, however, that cardiac arrest in poisoning by chloral hydrate, at least in the normal animal or human being, occurs secondarily to respiratory paralysis.

The circulatory depression occasioned by this drug has been shown to be due both to a direct paralyzing action on the muscle tissue of the heart and vessels and depression of the vasomotor center. With doses of moderate size or at the beginning of the effects of large doses there is shown a tendency to dilatation of the peripheral vessels, with resulting flush of the skin surfaces, which would suggest the presence of some special action on these vessels at a time when the internal (splanchnic) vessels and the heart are as yet but slightly influenced. Later, the splanchnic vessels and heart becoming depressed and the blood-pressure falling, the flush at the periphery subsides, and the pale, or cyanotic, clammy skin characteristic of ad-

vanced chloral intoxication is observed.

It is particularly the chlorine contained in chloral hydrate which is responsible for its tendency to depress the cardiovascular system. Any hypnotic containing chlorine shows the same tendency. But since the hypnotic effect of the drug is at the same time vastly increased through the presence of this element, the latter must be looked upon as a necessary evil in its chemical constitution.

*Respiration.*—Moderate doses of chloral hydrate cause slight slowing of the respiration, though this is scarcely greater than in ordinary sleep (Cushny). Large doses distinctly depress the respiratory centers in the medulla oblongata, the breathing becoming progressively slower, shallower, and sometimes irregular, until death finally takes place.

*Alimentary Tract.*—Here the effects of chloral hydrate reproduce those exerted on mucous membranes in general. Small doses, while causing a burning sensation in the throat and exciting the flow of saliva, act to some extent as sedatives in the stomach, especially if administered well diluted. Large or concentrated doses cause excessive local irritation and may produce nausea, vomiting, and purgation.

*Temperature.*—Chloral hydrate tends to reduce the body temperature, especially when given in large doses. This reduction arises both from the physical inactivity attending sleep, with consequent lessened metabolism and heat production in the muscles; the dilatation of the cutaneous blood-vessels, causing increased heat dissipation; in the later stages of poisoning from cardiac depression, with the



resulting circulatory inefficiency, and possibly also from diminished irritability of the heat-centers in the brain.

**Metabolism.**—In addition to lessening the consumption of oxygen and excretion of carbon dioxide by inducing muscular inactivity, chloral has been shown to produce qualitatively imperfect tissue metabolism. The amount of phosphates, nitrogen, and sulphur eliminated with the urine is increased—a fact which indicates augmented destruction of the nitrogenous elements in the tissues. The form in which the sulphur is excreted shows that the oxidation of proteins has been incomplete. Chloral hydrate, like chloroform, may produce, when freely used, fatty degeneration in various organs.

**Absorption and Elimination.**—As might be expected in view of its free solubility in water, chloral hydrate is rapidly absorbed through mucous membranes. Upon reaching the body tissues through the circulation, the drug is changed to trichlorethyl alcohol. This, in turn, enters into combination with the glycuronic acid normally present in the system, with resulting formation of urochloralic acid. The elimination of the drug takes place through the kidneys, chiefly in the form of urochloralic acid, but also in small part, especially where the amount of the drug taken has been large, as unchanged chloral. According to Sollmann, a small portion of the chloral is completely broken down in the system, being eliminated in the form of chlorides.

Chloral excretion occurs through the kidney. The forms in which it is excreted, *i.e.*, the relative amount of free chloral, trichlorethyl alcohol, etc., are obscure. With small doses, from 75 to 85 per cent. of the chloral

ingested is excreted, in dogs, within eighteen hours. As the dose increases, this percentage increases slightly. A breaking up of the chloral molecule, therefore, does not occur. Wallace (*Jour. of Pharmacol. and Exp. Therap.*, March, 1912).

**UNTOWARD EFFECTS AND POISONING.**—No unpleasant after-effects are, in general, experienced by the patient awakening from sleep induced by chloral hydrate. In some instances, however, a certain degree of dizziness and headache, together with mental torpor and general lassitude, are complained of. Where the dose used has been somewhat excessive, nausea and vomiting may occur. These symptoms may also appear earlier in the effects of the drug if it has been taken in too concentrated a solution. Flushing of the face, general hyperesthesia, and sometimes even mental excitement have been described as occasionally occurring under therapeutic doses before sleep is induced. Finally, hyperemia and swelling of the conjunctivæ, due to exudation of serum through the walls of the dilated ocular vessels, together with disturbances of vision, have been witnessed in certain individuals having an idiosyncrasy to the drug. In some, the conjunctival disturbance appears only where chloral and alcohol have been taken in combination.

Case of a paranoiac woman with great motor excitability in which 2 doses of chloral hydrate were given at an interval of twenty-four hours. A widespread eruption, consisting of dark-red macules and papules, with hemorrhage in places, developed after the second dose. Large bullæ appeared on the face, and the condition was associated with fever, pronounced sleepiness, and hemorrhagic conjunctivitis and bronchitis. Gregor (*Münch. med. Woch.*, April 23, 1907).

The chief untoward effect of chloral hydrate, however, is the production of circulatory and respiratory depression. This is, in reality, a typical manifestation of acute chloral poisoning, the consideration of which may now appropriately be taken up. Doses of chloral exceeding 1 dram (4 Gm.) soon induce profound sleep, from which the patient can only with difficulty be aroused. The spinal centers being also depressed, reflex action is diminished and peripheral sensation somewhat obtunded. Respiratory and circulatory depression makes its appearance in proportion to the toxicity of the dose. After ingestion of massive amounts, a condition closely analogous to complete general anesthesia is witnessed. The subject cannot be wakened, response to painful stimuli is abolished, the reflexes likewise, and the muscles are entirely relaxed. The respiration rapidly becomes slow and progressively shallower. The frequency of the heart beat is also lessened,—later, sometimes accelerated,—and the pulse becomes very feeble. The skin is pale or cyanosed, the forehead and upper limbs covered with moisture, the temperature of the body reduced, and death finally takes place from respiratory paralysis. The pupils in chloral poisoning are at first contracted, later dilated, as in the collapse stage of ether or chloroform narcosis.

The average fatal dose of hydrated chloral cannot be definitely stated; while the ingestion of as little as 15 grains (1 Gm.) has been followed by death, in a number of other instances amounts exceeding 400 grains (26 Gm.) have been taken without a fatal result.

Case of middle-aged man who was in a mental state bordering on melancholia due to worry and the use of alcohol. Chloral hydrate, 10 grains (0.6 Gm.), and potassium bromide, 15 grains (1 Gm.), were directed every three hours, with a double dose at bedtime. The prescription was written on Thursday, and the patient was not seen again until the following Monday. He was then found in bed with his knees and chin approximated; the extremities were cold, and he was jerking and rolling about. The breathing was slow and stertorous, the pulse slow and soft, the face ashen gray, with parched lips and swollen tongue; there was marked stupor. Since the prescription had been given he had had it filled four times, and had been drinking half a small glassful at a dose. During this time he had eaten heartily and had taken little or no alcohol. It is estimated that during the three days he had taken no less than 8 ounces of the mixture, or 640 grains (43 Gm.) of chloral and 960 grains (64 Gm.) of potassium bromide. Recovery was rapid under **strychnine**. P. F. Rogers (Med. Rec., March 10, 1900).

Case in which a large dose of this drug was taken without causing death. The patient ingested all of her sleeping medicine at one dose. It included 330 grains (22 Gm.) of chloral hydrate, 330 grains (22 Gm.) of potassium bromide,  $2\frac{3}{4}$  grains (0.18 Gm.) of extract of cannabis indica, and  $2\frac{3}{4}$  grains (0.18 Gm.) of extract of hyoscyamus.

The patient's condition when seen was as follows: pulse 62 per minute, and feeble; respiration 14; pupils contracted, face flushed, extremities cold; profound sleep, from which she could be aroused by violent shaking; she could not articulate a word. The treatment consisted of 5 drops (0.3 c.c.) of tincture of **nux vomica**, 1 teaspoonful of **brandy**,  $\frac{1}{2}$  teacupful of **hot, strong coffee**, and **bags of hot water** applied to the extremities until the limbs regained their natural tem-

perature. At each subsequent hour 2 drops (0.12 c.c.) of tincture of nuxvomica, and all of the hot, strong coffee that the patient could swallow (about 1 teacupful), were ordered given. Next day, twelve hours later, the patient could be aroused and could speak. The same treatment was continued. By the following day she had apparently recovered, without any bad effects. When last heard from she had been placed in an asylum.

Cases are on record in which 10 grains (0.65 Gm.) of hydrated chloral have produced death, as well as cases where 350 grains (22.5 Gm.) did not result in death. Acker (N. Y. State Jour. of Med., Nov., 1903).

The drug has been frequently used among the criminal classes as an accessory to robbery, viz., for the purpose of rendering unconscious intended victims. Thirty to 80 grains (2 to 5.2 Gm.) of chloral hydrate, generally incorporated in beer, constitute the so-called "knockout drops" in their usual form, and will render a person, especially if already partially intoxicated with alcohol, helpless for several hours. Occasionally, where the amount used has been excessive, death results.

The changes found *post mortem* in chloral poisoning include inflammation of the gastrointestinal mucous membranes, fatty changes in the parenchymatous organs, and clumping of the red blood-cells. None of these is constant or characteristic.

Experiments undertaken to determine what effects administration of chloral would have upon the liver and kidneys. Altogether 26 dogs were poisoned in various ways by chloral hydrate, and of these there were only 6 whose livers showed definite pathological changes. Chloral hydrate may occasionally produce fatty changes in the liver similar to those

caused by small doses of chloroform, but it is impossible to produce with this drug necroses in the liver like those found in delayed chloroform poisoning and eclampsia. The drug produces no histological changes in the kidneys. It causes an increase in the urinary nitrogen, which may be delayed until after recovery from anesthesia, and tends to return again to normal. J. G. Hopkins (Amer. Jour. of Obstet., April, 1912).

**TREATMENT OF ACUTE POISONING.**—Evacuation of the poison remaining unabsorbed should be secured, preferably by means of the **stomach tube**, or, if this be not possible, by an **emetic**. The use of emetics is attended with some danger, except in the early stages of poisoning, since the physical effort of vomiting may lead to exhaustion of the heart, the power of which is already reduced through the direct effect of the drug on this organ. The depression of the medullary centers will tend, at least in advanced poisoning, to interfere with the efficiency of centrally acting emetics such as apomorphine; hence, if an emetic be used at all, one acting peripherally, such as **zinc sulphate** or **copper sulphate**, should be employed.

From the start the patient should be kept at rest in the horizontal position in order to avoid overburdening the enfeebled heart. As in opium poisoning, **alternate hot and cold douches**, application of **wet towels** to the **face**, **slapping of the body with wet towels**, and **stimulation** by means of **electrical apparatus** or **flagellation** are of value to overcome somnolence and respiratory depression; but the patient should not be forced to walk, owing to the circulatory weakness.

Stimulants to the respiration, heart, and vasomotor system should be ad-

ministered, especially caffeine, in the form of **hot coffee** by the rectum or **caffeine-sodium benzoate** hypodermically in doses of 5 to 10 grains (0.3 to 0.6 Gm.), and **strychnine**,  $\frac{1}{20}$  to  $\frac{1}{10}$  grain (0.003 to 0.006 Gm.) hypodermically. To these may be added **aromatic spirit of ammonia** by the mouth; tincture of **digitalis**, 30 minims (2 c.c.); German **digitalin**,  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 Gm.), or **atropine**,  $\frac{1}{60}$  grain (0.001 Gm.) hypodermically.

**Heat** should always be supplied to the body from the exterior. Hot blankets, hot bottles or water-bags, skin friction, and even a hot bath may be employed.

In desperate cases intravenous infusion of normal **saline solution** at 110° F., with 10 minims (0.6 c.c.) of 1:1000 **epinephrin** solution added, should be thought of. **Artificial respiration**, to be started before spontaneous breathing ceases, and **inhalations of oxygen** complete the therapeutic measures available.

**CHRONIC CHLORAL HYDRATE POISONING** (Chloralism; Chloral Habit).—Continued use of this drug, usually for the relief of insomnia, leads in many instances to increased tolerance of it on the part of the system and subsequently to a condition of chronic poisoning associated with a series of more or less serious morbid phenomena. Among the earlier manifestations to appear are digestive disturbances, physical and mental enfeeblement, and eruptions on the skin or mucous membranes. The skin disorder is usually a purplish erythema, frequently upon the face; may occur either diffusely or in patches, and is probably due to the circulation in the blood of products of incomplete metabolism, to-

gether with continued relaxation of the superficial vessels. In some cases this relaxation is so marked that the blood-fluids pass through the walls of the engorged capillaries, edema resulting. Ecchymoses and ulcerations, including bedsores, may even occur. Other symptoms frequently seen are cardiac palpitation and sudden flushes of the skin. Dyspnea, the result of circulatory depression and occurring mainly after meals or on physical exertion, is a characteristic symptom. Insomnia is relieved only by further use of the drug, but overdosage of the latter is simultaneously a source of considerable danger, owing to the state of cachexia and defective powers of elimination. Nervous disturbances resembling those of chronic alcoholism, *e.g.*, mental dullness, loss of memory, hallucinations, tremor, and paralysis, may be noted. Death may finally occur from failure of the circulation.

In cases where the psychic disturbances due to the habitual use of chloral develops into a true psychosis, the condition of the patient resembles very closely the condition of normal sleep. The few sensory impulses that reach the patient's consciousness only provoke hallucinations and illusions. The functions of association are abnormally excited, and the patient rapidly changes from one subject to another. The sense of time disappears, and in a few minutes the patient lives through events that occupy years. A. F. Akopenko (Vratch, April 27, 1900).

Chloralism appears to be more common among women than men. As in all other forms of drug addiction, some previous neurosis will be found to precede the first use of chloral. The sleep which it produces is so profound and unaccompanied by unpleasant after-sensations that it is repeated as often as occasion calls

for it. Chloral can be taken secretly for a long time without any suspicion of its use. After a time the effect of its use appears in disordered digestion, irregular heart action, and increased nervousness and muscular unsteadiness. In persons past middle life a form of cardiac asthma with a tendency to delirium appears. These and many other obscure symptoms finally merge into delirium and death. Some observers have noticed that chloral-takers have peculiar blueness of the extremities, with venous congestion; also marked listlessness and lack of energy. The amount used varies from 20 to 2000 grains (1.3 to 130 Gm.) a day. Often considerable time will elapse before toxic symptoms appear; then, suddenly extreme prostration with delirium comes on, ending fatally. Sudden palsies, with vasomotor disturbances, heart-failure, and low states of delirium, should suggest chloralism, particularly if alcohol, opium, cocaine, and chloroform can be excluded.

When it is established that chloral addiction is present, the patient should be isolated at once and placed under positive restraint, and the drug withdrawn. Vegetable narcotics, such as **hyoscyamus**, **valerian**, **lupulin**, **bull-nettle**, and others of this class, may be given as substitutes, to be withdrawn at the earliest moment. Then comes the usual tonic treatment of **nux vomica**, **strychnine**, and **arsenic**. **Cinchona** and **iron** are also excellent drugs.

The insomnia and neuralgia with deranged nutrition which follow the withdrawal should be treated with **baths**, **foods**, and careful **hygienic management**.

Chloralism has been mistaken for general paralysis, neurasthenia, and hyperemia, as well as several affections of the cord. Many opium and alcohol cases are found to be complicated with chloral addiction, and their recovery is rendered more difficult. T. D. Crothers (Med. Standard, Aug., 1901).

Experiments in which gradually increasing doses of chloral were given daily by the stomach to dogs. At first the drug produces vomiting, but later the stomach becomes tolerant and vomiting does not occur. This local tolerance is common to gastric irritants. When large doses are given daily, a gradually increasing looseness of the bowels results, which eventuates in diarrhea. The chloral given, however, is absorbed. As far as symptoms of depression of the nervous system are concerned, only a slight degree of tolerance is obtained. After doses sufficient to induce narcosis are reached, the gradual increase in dosage still brings about complete narcosis, but its duration becomes less. The tolerance of the nervous system is not marked therefore, and is comparable to that from alcohol. As the dose is increased no change in metabolism, as measured by total nitrogen and urea excretion, is seen, and the animal maintains a fairly constant weight. After large daily doses the ammonia rises, however, and may reach twice the normal figure. The urine gives no qualitative reactions for acetone, or diacetic or oxybutyric acid. Albuminuria finally appears. The urine contains no sugar. The excretion of glycuronic acid runs fairly parallel to that of the chloral.

Although the change of chloral in the body to trichlorethyl alcohol and the pairing of this with glycuronic acid to form the inert urochloralic acid are of the nature of a protective mechanism, this cannot in itself bring about any marked tolerance for the drug, but rather is analogous to the power of the body-cells to destroy morphine in cases of morphine tolerance. Wallace (Jour. of Pharmacology and Exper. Therap., March, 1912).

**TREATMENT OF CHRONIC POISONING.**—Sudden withdrawal of chloral hydrate in those habituated has been known to result in a condition closely akin to delirium tremens, at-

tended with particular danger owing to the accompanying cardiac weakness; hence a gradual decrease in the amount of the drug taken is generally considered preferable. Meanwhile, stimulants to the circulation and nervous system, especially **strychnine**, should be given, and the enfeebled organism built up by means of a generous diet, an abundance of **fresh air**, and the administration of **iron**. **Cathartics** should be freely used in order the more quickly to rid the system of improper metabolic wastes.

#### **THERAPEUTICS. As Hypnotic.**

—Chloral hydrate is the strongest purely hypnotic drug now available, and surpasses all other agents of this class in certainty of action. Its ready solubility in water, prompt action, and general freedom from unpleasant after-effects combine to render it a most valuable drug. It is not, however, without disadvantages, chief among them being the readiness with which circulatory and respiratory depression are induced when a dose in excess of that actually needed for the hypnotic effect is administered or when cardiovascular disease or disease of the respiratory apparatus is present. Other, less salient, drawbacks include the irritant property of the drug, which renders its use by mouth inadvisable in gastric or intestinal inflammations, and the possibility of the formation of a habit when it is taken daily for any length of time.

In **insomnia** the result of increased nervous irritability, whether the latter be due to overwork, worry, toxemia, or occurs in association with insanity, chloral hydrate shows its greatest degree of efficacy. Where pain is present, on the other hand, its action

is greatly interfered with, as its pharmacological properties are not such as to exert distinct effects on sensation unless dangerously large doses are employed; for **insomnia** partly or wholly due to pain the administration of combined small doses of chloral hydrate and morphine is useful, a powerful hypnotic effect being thus obtained, while the unpleasant features of the action of morphine are minimized.

Large doses of chloral may produce a pin-point pupil. As the mechanism of the eye, peripheral to the ciliary ganglion, is not directly influenced by the chloral nor are the ciliary or sympathetic ganglia involved, the action must be central and due to removal of inhibitory influences which are normally active. Strychnine, caffeine, atropine and other centrally acting drugs are antagonistic to its action. Hyatt, McGuigan and Rettig (*Jour. Pharmacol. and Exper. Therap.*, July, 1920).

Whenever chloral hydrate is used alone in full doses the possibility of concomitant circulatory depression is to be kept in mind. It is in many cases advisable to guard against this effect by combining with the drug some stimulant, such as strychnine or digitalis (in case the latter is used, it should be given preferably an hour before the chloral, owing to the slowness of its action). Where the blood-pressure is already high, on the other hand, chloral hydrate, judiciously used, is likely to prove more effective as a hypnotic than other similar drugs which do not depress the circulation.

In **delirium** occurring early in the course of acute infectious diseases, as well as in **delirium tremens**, chloral may be relied on to exert a marked quieting influence, though special caution should be exercised in order

not to induce circulatory depression. In the infections, indeed, large doses are seldom necessary to procure the desired result. In delirium due to **poisoning by lead**, chloral is likewise valuable.

In 300 **scarlet-fever** patients treated with chloral hydrate during the febrile period, the drug being continued for several days after all fever subsided, an incidence of 5.5 per cent. of postfebrile nephritis was observed. In 756 patients treated without chloral, the incidence was 7.76 per cent. Chloral in some way protects the functioning part of the renal tissues in scarlet fever, greatly modifies the nervous symptoms, allays itching, and makes the patient more comfortable. In the author's experience it did not materially depress the circulation. The object in the chloral treatment is to administer the minimal amount of the drug necessary to produce light and continued somnolence, the dose being, of course, adjusted to the age and requirements of each case. The drug may be given in iced water every two, three, or four hours, if possible after food. B. F. Royer (*Therap. Gaz.*, Jan., 1907).

In various forms of **insanity** associated with excitement, such as **acute mania**, **agitated melancholia**, and **puerperal insanity**, chloral hydrate has been extensively used. As emphasized by Lloyd, the dose necessary for the production of sleep sometimes exceeds the limit of safety as regards the circulation; it is best, where small or moderate doses, such as 10 or 20 grains (0.6 or 1.3 Gm.), do not prove effective, to discontinue the drug. In mild, more continuous excitement or simple insomnia in these patients, trional or veronal are preferable.

**As Motor Depressant.**—By virtue of its paralyzing action on the motor functions of the spinal cord, chloral

hydrate diminishes reflex activity and is capable of arresting convulsive phenomena of all kinds. It has proven an extremely useful agent for this purpose. The dose required, however, is generally larger than that employed for the hypnotic effect alone.

In the convulsions of **strychnine poisoning** and **tetanus** chloral is a valuable sedative when given in doses of 30 or 40 grains (2 or 2.6 Gm.) or even more, in combination with 1-dram (4 Gm.) doses of potassium bromide. In the former disturbance the use of the more rapidly acting chloroform may render chloral hydrate unnecessary; it may prove useful, however, in prolonging the sedative action of the anesthetic after the latter has been discontinued. Rectal administration of chloral is frequently availed of in these cases.

Other disorders of a similar nature in which chloral has proven useful include **infantile convulsions**, **epilepsy**, **chorea**, **hiccough**, **uremic** or **puerperal convulsions**, **tetany**, **paramyoclonus multiplex**, **pellagra**, and **chronic ergotism**. In all instances a combination of the drug with bromides, which adds to the pre-eminently motor depressant effect of chloral sedation of the sensory nervous structures, is advantageous. In epilepsy and chorea the drug is, of course, indicated only in cases of marked severity, or, in the case of epilepsy, where the disturbance is chiefly nocturnal. In uremic and puerperal convulsions its calmative action is due partly to the lowering of blood-pressure induced. In **paralysis agitans** chloral may occasionally be required.

Chloral hydrate given by rectum to control convulsions in **eclampsia**

and allied toxemias of pregnancy. In treating a series of 20 eclamptic patients who had had one or more convulsions there was but 1 death—a mortality of 5 per cent., as compared with 28 per cent. in 251 previous cases in which chloroform was used for the same purpose. J. G. Hopkins (Amer. Jour. of Obstet., April, 1912).

In certain spasmodic conditions of involuntary muscle tissue, *e.g.*, in the **spasmodic laryngitis** of children, in **bronchial asthma**, and in **whooping-cough**, chloral hydrate is sometimes of service. In the first-named affection, 1 grain (0.06 Gm.) of chloral hydrate, combined with 3 to 10 grains (0.2 to 0.6 Gm.) of a bromide, may be given by rectum in water or milk (Abt). In pertussis Eustace Smith recommends chloral highly; he administers 1-grain (0.06 Gm.) doses every two to six hours, the longer intervals being allowed in very young children. In **incontinence of urine** chloral sometimes proves useful.

In the **vomiting of pregnancy** and in **seasickness**, chloral hydrate figures in the long list of available remedies. It is also frequently included in formulæ intended for the relief of **chordee**.

Chloral hydrate recommended in **seasickness**. As prophylactic, a full meal should be taken about an hour before embarking and a recumbent posture then maintained. Vomiting in seasickness is probably of central origin and the result of cerebral anemia, due in turn to constriction of the arteries of the head owing to the motion of the ship. When seasickness develops, therefore, chloral hydrate, which will dilate the cerebral vessels, should be given. Binz (Centralbl. f. inn. Med., Feb. 28, 1903).

Palvy used chloral hydrate in doses of 15 to 25 grains (1 to 1.6 Gm.) per

rectum in 15 cases of **hemoptysis**. A favorable effect was produced within one-half to three-quarters of an hour.

In obstetrics chloral hydrate has been used to promote relaxation of the cervix in cases of difficult parturition. It is also stated to relieve pain in the early stages of labor (Woodbury).

As a preliminary to chloroform anesthesia, chloral hydrate has been employed with asserted advantage by Delbet and Dupont.

Report made on 850 cases of **chloroform anesthesia** in which chloral hydrate was used. In doses of 60 grains (4 Gm.) the drug was found non-poisonous. It greatly reduced or prevented the stage of excitement before anesthesia, and hastened the induction, anesthesia being usually complete within ten minutes in men and within eight minutes in women,—an advantage of several minutes over scopolamine-chloroform anesthesia. The incidence of vomiting was uninfluenced. P. Delbet and R. Dupont (Rev. de chir., June, 1910).

**As Vasodilator.**—The tendency of chloral hydrate to paralyze the smooth muscle tissue in the vascular walls renders it a vasodilator. This property is sufficiently marked to lead to occasional use of the drug specifically to lower blood-pressure. Thus, 3-grain (0.2 Gm.) doses have been given for this purpose in **arteriosclerosis**. The hypotensor effect is especially useful as an adjuvant to the production of sleep in cases with high blood-pressure. The drug is considered indicated especially where nitrites are not well borne.

**Local Uses.**—The combined analgesic, rubefacient, and antiseptic properties of chloral hydrate form the basis of its local uses. It is sometimes employed to relieve itching, as



**in pruritus, eczema, etc.** In **urticaria** the use of the following combination has been recommended:—

℞ *Chlorali hydrati*,

*Acidi borici* .....āā gr. xx (1.3 Gm.).

*Aqua camphora* .... f3ij (60 c.c.).

M. Sig.: For local use.

For antiseptic and analgesic purposes a 1 to 5 per cent. solution of the drug may be applied with advantage to **discharging ulcers** or **wounds**, **carcinoma** of the **uterine cervix**, **bed-sores**, **cracked nipples**, etc. The slight additional irritating action exerted under these circumstances tends to favor healing through local stimulation. The use of a 20 per cent. solution of the drug has been recommended in **anal fissures**, and that of a 2 per cent. solution in **hyperidrosis** and **bromidrosis**. In the external treatment of parasitic skin diseases, *e.g.*, **ringworm**, chloral in 5 per cent. solution may also be used.

In concentrated solution or as a powder—sprinkled over adhesive plaster, which is to be warmed and laid on the skin—chloral is capable of producing blisters. In diabetes, where vesication is required and cantharides cannot be used, Lépine has found a mixture of chloral hydrate ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains—0.05 to 0.1 Gm.—to the sq. cm. of surface) and tragacanth of special value.

When a prompt and marked vesicant effect is required, chloral hydrate is better than cantharides and has none of its disadvantages. With children it is next to iodine, the counterirritant of choice. It will produce erythema, vesication, or ulceration, as desired. M. T. Brennan (Montreal Med. Jour., May, 1902).

A mixture in equal parts of chloral, menthol, and camphor, ground to-

gether until a fluid is formed, constitutes an especially convenient and effective preparation for securing a counterirritant effect and consequent relief from pain in **neuralgia**, **lumbago**, and other similar affections, as well as for application to **mosquito-bites** or **flea-bites**. Chloral camphoratum, a semiofficial preparation (National Formulary) consisting of equal parts of chloral and camphor triturated in a warm mortar, is adapted for the same purposes. Chloral-menthol and chloral-thymol differ little from chloral-camphor. Where additional local analgesic power is required, a small amount of cocaine, *e.g.*, 1 part in 50, may be added to these combinations.

A very efficient anodyne embrocation may be made as follows:—

℞ *Chlorali hydrati* .... 3j (4 Gm.).

*Camphora* ..... gr. lxxv (5 Gm.).

*Glycerini* ..... f3iv (16 c.c.).

*Alcoholis* ..... f3iij (12 c.c.).

*Olei juniperi* ..... f3ss (2 c.c.).

Mix and heat gently until solution is effected. Keep well stoppered.

Instead of the fluid preparations just mentioned, an ointment may be employed, such as the following:—

℞ *Chlorali hydrati*,

*Camphora* .....āā 3j (4 Gm.).

*Petrolati* ..... 3j (30 Gm.).

M. Sig.: Apply locally.

The action of liniments intended for counterirritation, *e.g.*, chloroform liniment, may be enhanced by the addition of chloral hydrate.

As a dental anesthetic, G. T. Maxwell uses the following:—

℞ *Chlorali hydrati* .. 3iss (6 Gm.).

*Tinctura lavan-*

*dula* ..... f3ss (15 c.c.).

*Aqua rosa*,

q. s. ad ..... Oj (0.5 liter).—M.

A small quantity of this solution, held in the mouth, overcomes offensive odors from putrescent blood and tissues, and quickly hardens the gums. It is also useful as a deodorant in the presence of decayed teeth, and gave the author satisfaction in the treatment of syphilitic pharyngeal ulcers.

Chloral hydrate recommended to overcome the foul odor in gangrene of the lung. The patient should wash the mouth out after coughing with a dilute solution of the drug. By placing a tablespoonful of a 1 to 3 per cent. solution of chloral hydrate in the sputum flask, odor from it will be entirely obviated. A. Siegmund (Therap. Monatsh., July, 1909).

Chloral hydrate found of great value in tonsillitis and pharyngitis. A thimbleful of a 2.5 per cent. solution should be taken into the mouth, the head thrown back, and the solution worked about by masticatory movements and movements of the head from side to side, without gargling. After continuing this some time, the solution should be spat out, the head thrown back again, and the remaining fluid thus caused to act on the deeper mucous membranes. The procedure should be repeated every half-hour. In mercurial stomatitis, a 2 per cent. solution may be sprayed on the gums, and at the same time a mouth-wash of 1 per cent. solution prescribed for frequent use. In chronic laryngitis a fine spray of 1 per cent. chloral hydrate is also useful. In nasal diphtheria when the secretion is profuse and purulent a 1 per cent. solution in normal saline forms a satisfactory nasal wash. In addition to the mechanical cleansing effect, chloral hydrate insures disinfection and deodorization, and, following the initial burning, a decrease of pain. Heller and Quinke (Münch. med. Woch., Nov. 23, 1909).

It has been claimed that if a strong solution of chloral hydrate be painted

on warts or corns gradual disappearance of the lesions will follow. The application of a 25 per cent. solution is recommended for aborting furuncles.

According to Bonatti, a combination of chloral with senna constitutes a prompt, reliable, and powerful purgative which will be found effective even where jalap and croton oil have failed:—

℞ *Infusi sennæ*. f3x (300 c.c.).  
*Chlorali hydrati* ..... gr. xxiv-xlv (1.5-3 Gm.).  
*Syrupi* ..... f3j (30 c.c.).—M.

As a preservative for urine and anatomical specimens, chloral hydrate has been found very effective. Heller recommends a 5 per cent. solution for the removal of odor from the hands after post-mortem examinations.

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**CHLORALFORMAMIDE** (*Chloralformamidum*; "Chloralamide"; Formamidated Chloral).—This is a hypnotic drug having the chemical composition  $\text{CCl}_3\text{CH}(\text{OH}).\text{CONH}_2$ . It is essentially a combination of chloral with the stimulating substance formamide ( $\text{HCONH}_2$ ), and is made by the direct union of these two constituents. The name "chloralamide," hitherto frequently applied to this drug, is a misnomer, as the true chloralamide has the composition  $\text{CCl}_3\text{CH}(\text{OH}).\text{NH}_2$ . Neither should this substance be confused with chloralimide, or  $\text{CCl}_3.\text{CH}:\text{NH}$ , which has also been employed to a slight extent as a hypnotic.

Chloralformamide occurs in the form of colorless, shining, odorless

crystals, having a somewhat bitter taste. These crystals melt at  $115^{\circ}$  C., and if further heated undergo decomposition. The drug is slowly soluble in 18.7 parts of water, more rapidly in 30 or 40 parts of water, and in 1.3 parts of alcohol at ordinary temperatures, and also dissolves readily in glycerin and ether. Its dissolution in water is hastened by the addition of a small amount of dilute hydrochloric or sulphuric acid. It keeps well in solution, provided no heat be applied; if the solution be heated to  $60^{\circ}$  C. ( $140^{\circ}$  F.) the drug is decomposed by hydrolysis, chloral hydrate and formamide being set free.

**DOSE.**—The average dose of chloralformamide was officially given as 15 grains (1 Gm.). But in general, this substance may be considered to act only two-thirds or even one-half as powerfully as chloral hydrate, and the dosage employed regulated in accordance with this fact. Since the drug is not used to subdue convulsions, 45 or 50 grains (3 to 3.3 Gm.) need rarely be exceeded. It is no longer official.

Halász took experimentally for two days 15 grains (1 Gm.) of the drug, without any noticeable effect; when 30 grains (2 Gm.) were subsequently taken, the hypnotic action became evident, and, when 45 grains (3 Gm.) were ingested on arising, sleep occurred in the morning.

**PHYSIOLOGICAL ACTION.**—Chloralformamide exerts a hypnotic effect by depressing the brain centers. Its action is essentially that of chloral hydrate (*q.v.*) modified by the addition of formamide. The resulting differences consist chiefly in a weaker action on the spinal cord and a less tendency to depress the circulation than is the case with chloral

hydrate. Experimentally, chloralformamide has shown itself incapable of lowering the blood-pressure like chloral hydrate except in massive doses, the stimulating effect of the formamide evidently counteracting the tendency of chloral itself in this direction. Wood and Cerna found the respiratory rate considerably increased by chloralformamide in animals. The drug suffers by comparison with chloral, however, in respect of rapidity and certainty of action. That it cannot be relied upon to the same degree as chloral hydrate would seem to be shown by the fact that it has not displaced the latter in the favor of the profession, even for pure hypnotic purposes.

Chloralformamide, before exerting its effects, is slowly split up in the organism into its two constituents, chloral and formamide, and this accounts for the slowness of its action. The chloral undergoes further the customary reduction to trichlorethyl alcohol and is eliminated in the form of urochloralic acid.

According to Bilhaut, chloralformamide does not accumulate in the system until after six weeks of constant employment, every other day.

**UNTOWARD EFFECTS.**—Unpleasant side- or after- effects seldom accompany the use of chloralformamide. J. Wood, in 280 cases, noticed no untoward results even when the use of the drug was continued for ten days. Chapin, however, observed that, in cases where chloralformamide failed to produce sleep, headache, nausea, vomiting, dizziness, and depression were very likely to occur. Dryness of the throat is complained of in some cases. Adolph Robinson observed that the drug occasionally

produced restlessness for a short time. Among 50 cases in which chloralformamide was used by Toulmin, 4 experienced a sensation of being dazed and confused, while 2 showed mental derangement. Cases in which a skin eruption was produced by this drug have been reported by Yeo, Umpfenbach, and Springthorpe.

**THERAPEUTIC USES.**—In addition to being safer than hydrated chloral in regard to possible circulatory depressant effects, chloralformamide possesses the advantage of being less unpleasant to take and less irritating to the stomach. It may be administered in capsules, though a solution, such as the following, is preferable, acting more rapidly:—

℞ *Chloralformamidi* ..... ʒiij (12 Gm.).  
*Acidi sulphurici aromatici* ..... ℥x (0.6 c.c.).  
*Syrupi* ..... fʒss (15 c.c.).  
*Aqua destillata*, q. s. ad fʒiij (90 c.c.).

M. Sig.: Take two teaspoonfuls in water an hour before retiring.

An alcoholic preparation may also be prescribed:—

℞ *Chloralformamidi* ..... ʒij (8 Gm.).  
*Tr. cardamomi comp.*,  
*Syrupi aurantii* ..... āā fʒj (30 c.c.).

M. Sig.: Two teaspoonfuls an hour before retiring.

Or,

℞ *Chloralformamidi* ..... ʒij (8 Gm.).  
*Spiritus vini gallici*,  
*Syrupi rubi* ..... āā fʒj (30 c.c.).

M. Sig.: One teaspoonful at a dose. (Clevenger.)

An enema of chloralformamide may be given, according to Lettow, as follows:—

℞ *Chloralformamidi* . gr. xlv (3 Gm.).  
*Acidi hydrochlorici diluti* ..... ℥ij (0.12 c.c.).  
*Alcoholis* ..... ℥xv (0.9 c.c.).  
*Aqua destillata* ... fʒiij (90 c.c.).—M.

In simple **insomnia**, unaccompanied by pain, chloralformamide is a useful substitute for chloral hydrate, though the slowness of its action is somewhat of a disadvantage. That the drug is more efficient than chloral where pain is present has been maintained by some, but it does not seem likely that this is the case, in view of the close similarity in chemical composition of the two substances. According to Kny, sleep induced by chloralformamide is more refreshing than that caused by chloral hydrate.

Chloralformamide is a safer hypnotic in cases of heart disease than hydrated chloral, and has even been employed to relieve dyspnea in these patients. The dosage should be moderate, as Robinson found in 3 cases of valvular disease that 30-grain (2 Gm.) doses produced acceleration and weakening of the pulse.

Sir Clifford Allbutt considers this drug the best among the milder hypnotics for use in heart disease, though where there is great distress it is likely to prove inefficient. In the precipitate heart action which sometimes accompanies cardiac involvement in **influenza**, this author uses 5 to 10 grains (0.3 to 0.6 Gm.) of chloralformamide in combination with a few drops of belladonna tincture.

In the sleeplessness of insane patients, *e.g.*, in **mania** and **melancholia**, chloralformamide has also been recommended, although F. W. Robertson has recently reported it as being without effect in cases where veronal, trional, and sulphonal proved useful. According to Clevenger, it is most effective in the psychoses accompanied by depression.

Browning employed the drug with good results to diminish nervous-

ness in cases of excessive irritability engendered by cigarette-smoking.

In **delirium tremens** Simpson found chloralformamide useful in the stage immediately preceding an actual outbreak.

In **chorea** the sedative action of this drug has also been found useful by some observers. Thus, Alt reports a case in which, after arsenic had failed to cure in fourteen weeks, administration of chloralformamide in doses of 15 grains (1 Gm.) three times daily caused almost complete cessation of the movements in eight days. Steele obtained similar results.

In combination with potassium bromide (30 grains, or 2 Gm., of each drug), chloralformamide has been recommended as a prophylactic for seasickness. The stomach should be empty when it is taken for this purpose.

Finally, Whitmore has praised the drug as being useful in **pulmonary tuberculosis** not only to bring on sleep, but to lessen cough, facilitate expectoration, and check night-sweats.

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**CHLORALOSE** is a hypnotic drug made by heating anhydrous chloral with glucose (grape-sugar). It is not official. Chloralose occurs in the form of colorless crystals, which have an unpleasant, bitter and acrid taste.

Chloralose is only slightly soluble in cold water (1 in 200 parts), but dissolves more readily in hot water and very easily in alcohol or ether.

**DOSE.**—The dose of chloralose is 3 to 10 grains (0.2 to 0.6 Gm.). Small doses, such as 3 or even 2 grains (0.2 or 0.13 Gm.), should be used at first. If sleep is not induced, an additional 3-grain (0.2 Gm.) dose may be given (Morrill).

**PHYSIOLOGICAL ACTION.**—Chloralose resembles hydrated chloral in its action on the brain, inducing sleep by depression of the psychic centers. The spinal cord, however, is excited by it rather than depressed; during sleep induced by chloralose the reflexes may be found exaggerated, and in experiments on animals even convulsive phenomena are frequently observed. According to Marandon de Montyel, moreover, the depressant action of this drug on the brain itself may be preceded by slight, fugacious excitation. This effect is readily observed in the lower animals, dogs in particular showing a preliminary period of excitement (Cappelletti). Even during unconsciousness the cerebral cortex has been found abnormally irritable. While a dog under the influence of the drug is insensible to pain, and will lie still while operations are performed on the skin, muscles, and even bones, a sudden jerk of the table or floor will make him leap violently into the air (Henriot and Richet).

The hypnotic effect in man is occasionally preceded by muscular twitchings or tremors, with dizziness and difficulty of speech. Once the sleep comes on, however, it is often more profound than normally, the subject becoming insensible to pinching of the skin, and the corneal reflexes being apparently quite abolished (Chambard).

Upon the circulation, respiration, and body temperature chloralose exerts little or no depressing effect except in toxic doses. De Montyel finds that during the period of psychic sedation (i.e., just preceding sleep), accompanied with motor hyperexcitability owing to the spinal stimulation, there occurs an increase of the respiratory rate, temperature, and blood-pressure, together with a diminution of the pulse rate. The drug is capable, however, of producing a periodical type of respiration.

An increase of appetite has been stated to occur after the use of chloralose. According to De Montyel, the amount of urine passed is temporarily increased by it; Lombroso and Marro, on the other hand, have stated that it diminishes the amount of this fluid and increases its specific gravity.

**UNTOWARD EFFECTS.**—Numerous cases in which unpleasant side-effects occurred have been reported. The chief phenomena witnessed have been nervous, consisting of motor disturbances such as tremor, epileptiform convulsions, and catalepsy, and psychic disturbances such as amnesia, delirium, and vertigo. Bardet, after giving 3 grains (0.2 Gm.) to a 6-year-old child, witnessed a cataleptiform condition lasting two hours. The same dose, given to a woman by Féré, produced paresthesia and loss of motor control over the limbs. Nausea, vomiting, restlessness, incoherence, and involuntary evacuation of urine and feces were observed by Touvenaint in two patients after 6-grain (0.4 Gm.) doses. Temporary amnesia appears, along with evidences of spinal excitation, to have occurred with especial frequency as an unfavorable effect of chloralose.

Rendu and Herzen have reported cases, both in tuberculous patients, in which doses of 4 and 3 grains (0.26 and 0.2 Gm.), respectively, produced symptoms of collapse, with unconsciousness and convulsive movements.

Other untoward effects reported include diplopia, foaming at the mouth and reddening of the face, continued passing of the hands over the face, head, and neck, and, in a case reported by Lombroso, respiratory depression.

**THERAPEUTIC USES.**—The advantages of chloralose as a hypnotic, viz., fairly prompt and powerful action, relative lack of depressing effects on the circulation, and absence of gastrointestinal irritation or subsequent headache, appear to be rather more than counterbalanced by its disadvantages, i.e., tendency to spinal excitation, uncertainty as to the dosage required for the desired degree of effect, and unpleasant taste. The last-named disadvantage can, however, be partly overcome by the addition of some strong aromatic flavoring agent to the solution in which it is given, or by its administration in cachets. Tyson considers it important for certainty of effect and avoidance of unpleasant results from subsequent doses that the drug be given in solution, preferably in hot water or milk. If a cachet is used, it should be followed

by water. Hoest has sometimes given the drug mixed with solid food.

In certain classes of cases the drug is plainly to be avoided, *e.g.*, where there is already excessive spinal irritability, as well as in somnambulism and in cases of advanced pulmonary tuberculosis. In hysteria Goldenberg advises caution in the use of the drug, as these patients are very susceptible to it.

When it is used the patient's relatives should be warned of the possibility of the occurrence of apparently alarming, but relatively harmless, side-effects.

According to Tyson, the drug is best adapted for the **simple insomnias**. It acts more rapidly than any other ordinary hypnotic except morphine, is efficient in much smaller doses than chloral hydrate, and often acts well in obstinate cases where other hypnotics have failed. The maximal dose should be 5 grains (0.3 Gm.); this may have to be repeated, in not less than an hour. Smaller doses, however, should be used before resorting to this one. Khmielefski states that the amount required to produce sleep varies much in different cases and at different times in the same person. Where there is any gastrointestinal disorder, chloralose is almost the only hypnotic which can be given for a prolonged period without harm.

Haskovec, who administered the drug in 82 insane patients in doses of from 1½ to 15½ grains (0.1 to 1 Gm.), obtained the best results in cases of **mania**, **epilepsy**, and **alcoholism**. Flemming, on the other hand, while regarding the drug as beneficial in the insomnia of **psychical excitement**, **neurasthenia** and overwork, functional cardiac irritability, and epilepsy, found it of no avail in the insomnia of alcoholic excitement, multiple neuritis, cerebral hemorrhage, or that due to any painful organic lesion. Lombroso and Marro, giving chloralose 15 times to 3 insane patients, found that at first sleep always followed a dose of 4 grains (0.25 Gm.), but that later the amount had gradually to be increased. Féré used 12-grain (0.75 Gm.) doses in a case of **chorea**. The movements disappeared and the drug produced no gastric trouble, although given continuously for several weeks. S.

**CHLORAMINE.** See WOUNDS.

**CHLORATE OF POTASSIUM.**

See POTASSIUM.

**CHLORBUTANOL.** See CHLORETONE.

**CHLORETONE** (chlorbutanol; acetone-chloroform) is an unofficial drug allied to chloral hydrate and constituted chemically as trichlor-tertiary-butyl alcohol:  $\text{CCl}_3\text{C}(\text{CH}_3)_2\text{OH}$ . It is made by slowly adding potassium hydroxide to a mixture in equal weights of acetone and chloroform, then removing any excess of the reacting agents and distilling the remaining fluid with steam. It occurs in the form of white crystals having an odor and taste very similar to those of camphor. Chloretone is only sparingly soluble in cold water (0.8 to 1 part in 100 parts of water); it dissolves more readily in boiling water or in glycerin, and is freely soluble in alcohol, ether, chloroform, acetone, benzine, glacial acetic acid, and oils. Like chloral hydrate, chloretone is volatile at ordinary temperatures. To an aqueous solution of chloretone the terms ancon or anesin have been applied.

**DOSE.**—The dose of chloretone is 2 to 20 grains (0.12 to 1.25 Gm.). The average dose for hypnotic purposes may be stated as 10 or 15 grains (0.6 to 1 Gm.), while that for gastric sedation may vary from 2 to 15 grains (0.12 to 1 Gm.).

**PHYSIOLOGICAL ACTION.**—Chloretone possesses marked local anesthetic properties, far surpassing those of chloral hydrate, though hardly comparable with those of cocaine. It is superior to cocaine in being distinctly antiseptic and showing no tendency to produce local sloughing or swelling (Leo).

Blood-serum and other organic fluids can be preserved indefinitely by saturation with the drug (Houghton and Aldrich). Its efficiency in the preservation of other remedies, *e.g.*, epinephrin, is also widely availed of.

The general physiological effects of chloretone greatly resemble those of chloral hydrate (*q.v.*). Of the central nervous system, the brain is the only portion depressed by moderate doses. Sleep is produced, which deepens to profound

torpor as the dosage is increased. Complete general anesthesia results from the administration of large doses.

On the circulation chloretone usually has little or no effect, at least for a time, even in doses sufficient to produce general anesthesia. Frequent use is made of this property in experiments on animals. In a dog deeply under the influence of chloretone, the blood-pressure, pulse, and respiration often remain unchanged for hours. The animal does not, however, recover from the effects of the drug, for after a prolonged period of safety the respiration and pulse rate become progressively slower, the blood-pressure descends, and death takes place from respiratory failure. Where a dose insufficient to induce anesthesia has been administered, the animal, upon recovery from the hypnotic effect, may exhibit inco-ordination lasting for two or even three days. The drug exerts a powerful effect upon the body temperature, which may be lowered even before the animal becomes drowsy (Rudolf). According to Impens, there is simultaneous lessening of oxygen consumption. In the rabbit the fall in blood-pressure is produced sooner than in dogs (Sollmann).

The absorption of chloretone is fairly rapid, but its elimination is slow. In animals poisoned with sublethal amounts, a marasmic state may remain after recovery from the acute effects.

**UNTOWARD EFFECTS.**—Unpleasant results from the use of chloretone in moderate doses as a hypnotic have seldom been reported. The undesirable effect most frequently attributed to it is headache, which, however, occurs chiefly after excessively large doses. Hutton has noticed an idiosyncrasy in a small proportion of persons who are always unpleasantly affected by the drug. In a case of vomiting of pregnancy in which he employed it, the patient complained much of giddiness.

Donald has recorded the case of a morphine habitué, suffering from insomnia and great depression, partly by reason of abscess present in various parts of the body, who took one night 24 grains (1.5 Gm.) of the drug, the next day 48 grains (3 Gm.), and the third day 120 grains

(8 Gm.). On the following morning the patient was in a profound sleep, but when roused was able to speak, and drank water with avidity, though refusing food. He was able to walk to the bathroom, though co-ordination was impaired. A mild general anesthesia persisted for two days, and sleep persisted almost continuously for six days. The pulse and respiration were slow, and toward the end of the week the temperature became subnormal. No other unfavorable effects were noted except vomiting; that the drug had directly caused this symptom, however, was doubtful.

**THERAPEUTIC USES.**—As a hypnotic chloretone has been employed in doses of 5 to 15 grains (0.3 to 1 Gm.). According to Ward, 5 grains of chloretone are immediately dissolved by 1 dram (4 c.c.) of alcohol, and the drug is best given in this way—in alcohol or whisky—followed by a glass of milk. Houghton and Aldrich state that the drug has proven especially useful in persistent **insomnia** of the aged and in cases accompanied by high blood-pressure. Although chloretone has the decided advantage of not irritating the gastrointestinal tract, the consensus of opinion appears to be that its hypnotic effect is not as strong as that of hydrated chloral, and that the use of sufficient amounts to produce narcosis is attended with greater danger than in the case of the older drug. Hutton states that he has not been favorably impressed with chloretone as a hypnotic; doses of 15 and 20 grains often failed to give sleep, and caused heaviness or bad taste in the mouth next morning.

Chloretone employed in 50 cases in which **sleeplessness** was an important symptom. In 5 cases of **neurasthenia** 20 grains (1.3 Gm.) at bedtime generally produced refreshing sleep lasting from six to eight hours. In 2 of these, opium had given rise to excitement, and chloralamide and trional failed. In **chronic heart disease**, where the symptoms were not severe, chloretone was useful. In **chronic nephritis** it generally gave good results. In 1 case, that of a middle-aged man with **uremic delirium**, it was given every night for

two weeks, and it rarely failed to give the patient sleep of at least three or four hours' duration. In several cases of pneumonia, with moderate fever, the results were not satisfactory, and in delirium tremens the drug was less efficacious than paraldehyde, bromides, or hyoscine, though in 1 case, where the delirium developed while the patient was under treatment for compound fracture of the leg, it acted well. Twenty-grain (1.3 Gm.) doses always exerted a quieting effect, and would generally induce sleep of from five to six hours' duration. In **phthisis** the results were very favorable. In **typhoid fever** the drug was especially valuable in convalescence. In 1 case of **morphine addiction** in which the daily dose did not exceed 2 grains (0.13 Gm.), the drug was employed with satisfactory results. It is seldom successful in the presence of fever, at least when the temperature rises above 102° or 103°. A. A. Stevens (N. Y. Med. Jour., Feb. 23, 1901).

Ward gave 2½-grain (0.15 Gm.) doses of chloretone in brandy to a child 4 years of age suffering from **whooping-cough**. The nocturnal coughing paroxysms were thereby arrested. In **epilepsy** and **tetanus**, the drug has also been used.

Chloretone may be prescribed, like bromide of potassium, for **nervous hyperexcitability**. It exerts a preventive influence over the epileptic attack, although from experience with it the author cannot conclude that it has a curative effect. It is useful in various **mental diseases**, especially in **acute mania**, and in general in all cases in which the cerebral excitomotor function was altered. Vento (Revista de Med. y Cir. de la Habana, Aug. 25, 1908).

Chloretone used in a case of **tetanus**, with recovery. The patient had first been placed on large doses of bromide and chloral without any effect; on the second day a rectal injection of chloretone, 30 grains (2 Gm.), in olive oil, 2 drams (8 Gm.), was given, and this was followed by thirteen



further daily injections of 20 to 30 grains (1.3 to 2 Gm.). Except for chloral and bromide on the first, seventh, and thirteenth days, no other drug was given but chloretone, and no antitetanic serum was injected. The relief of trismus enabled the patient to take nourishment and maintain his strength. V. St. John Croley (Indian Med. Gaz., Sept., 1911).

The most important use of chloretone is as a local analgesic. When applied in aqueous solution (1 per cent.) to open **wounds** or abraded surfaces it is very effective in lessening discomfort and in addition tends to exert an antiseptic effect. For **burns, scalds, or painful ulcers** it may be used with advantage, either as a powder in admixture with 1 to 10 parts of finely divided boric acid or as an ointment of 10 per cent. strength. According to Siter, chloretone does not delay union in wounds. He has used the drug with satisfaction as a powder in cases with **condylomata, varicose ulcers, chancroids**, as well as for infected wounds.

As a palliative in **toothache**, a mixture of equal parts of chloretone and camphor, together with a small amount of oil of cloves, has been recommended; it should be applied by means of cotton, which may with advantage be introduced into the cavity, if there be one.

In the removal of foreign bodies from the eye, H. M. Morton has found chloretone of value as an analgesic. He prefers its use to that of boric acid in **conjunctival inflammations** and **dacryocystitis**. Although its local anesthetic effect in the eye is quite superficial, it is prompt, and neither the pupil nor accommodation is affected.

According to Hill, a saturated solution of chloretone in 15 per cent. alcohol, used hypodermically, induces a localized anesthesia sufficient to permit of minor operations, while a mixture of chloretone and ether in equal parts is still more powerful, and is particularly useful to dentists for application to nerve-pulps before removal of the latter. This author also points out the utility of a chloretone solution for the relief of pain following strong injections in **cystitis**.

In **dysphagia** and in various **respiratory affections** the use of oily solutions of chloretone or of insufflations of chloretone vapor has been recommended.

Local application of an oily solution of chloretone in the treatment of **dysphagia** from various causes highly recommended. A 10 to 20 per cent. solution in olive oil or almond oil is used. The effect lasts two to three hours, and in general it is not necessary to use the applications oftener than three or four times a day. No disagreeable by-effects follow. The solution was employed in simple as well as in **lacunar and follicular tonsillitis**, in **diphtheria**, in **syphilitic ulcers of the tonsils and throat**, in **tuberculous ulcers of the epiglottis**, etc. In almost all cases there was diminution of the pain and improvement in swallowing, while in acute infectious processes the applications were also valuable on account of the antiseptic properties of the drug. The most distinct action was observed in lacunar and follicular tonsillitis. Jaquet (Corr. f. schweizer Aerzte, Nov. 1, 1904).

New method of applying chloretone to the mucous membrane of the throat described. By application of heat chloretone is readily liquefied and its vapor can be deposited upon a surface by a current of air. All that is necessary is a glass tube, with a spherical bulb at about the center of the tube. About 10 grains (0.65 Gm.) of chloretone are placed in the bulb, the opening in the top is closed by a cork, and heat applied until the crystals melt. An alcohol lamp, gas flame, or even a lighted match will supply the necessary heat. While the chloretone is in the liquid state a current of air is passed through the glass tube from a compressed-air apparatus or an ordinary atomizer bulb.

The chloretone vapor deposited upon the mucous membrane at first forms a white film, then gradually it becomes dissolved. At first there is a slight tingling, and a suggestion of the taste of camphor, which is soon followed by anesthesia.

Chloretone thus applied to a **tuberculous larynx** will produce in a few minutes anesthesia sufficient to enable a patient to swallow soft food without discomfort and often lasting for hours. It was used similarly to relieve pain following operations upon the throat, and in malignant disease. Its effects wear out in time, but it can be used in increasing frequency without danger of a drug habit or poisonous effects. Fiocre (*Presse médicale*, July 20, 1907).

The writer advocates **rectal anesthesia** by means of chloretone for operations around the head, neck, and chest, where the element of fear is in evidence. He prepares the rectum by giving a cathartic the evening before, followed by enemata and suppositories of chloretone to anesthetize the rectal mucosa. Twenty minutes after the insertion of the chloretone, morphine and atropine are given hypodermically and 20 minutes later a mixture of oil and ether is introduced, in the proportion of 50 to 75 per cent. of ether and 50 to 25 per cent. of oil. One ounce (30 c.c.) of the mixture is given for every 20 pounds of body weight, not to exceed 8 ounces (240 c.c.), through a rectal tube at the rate of 1 ounce (30 c.c.) a minute. In from 10 to 55 minutes the patient goes to sleep. The length of the anesthesia varies from 2½ to 3 hours, but it may be shortened or lightened by withdrawal of the mixture through a rectal tube. After operation the bowels are massaged and cold water irrigations given to remove the oil and ether. Intravenous injections of normal saline solution may be given if the anesthesia is too deep. M. A. Leavitt (*New Eng. Med. Gaz.*, li, 248, 1916).

That the drug, taken internally, exerts an anesthetizing effect upon the gastric mucous membrane is shown by the experiments of Houghton and Aldrich, who found that after its administration to dogs mustard failed to induce emesis, although on subsequent post-mortem examination the usual changes in the mucosa resulting from irritation by the mustard were ap-

parent. This property has led to the use of chloretone for the relief of pain in **gastric carcinoma**, **ulcer**, and **gastralgia**, as well as for the purpose of subduing vomiting, as in **seasickness**, **vomiting of pregnancy**, etc. Porter found, in a case of **acute alcoholic gastritis**, that in spite of the vomiting of food the patient retained chloretone without difficulty and steadily improved under its influence.

Chloretone employed in 6 cases of **vomiting in pregnancy**. In 4 the nausea and vomiting was at least so far controlled as to become unimportant and no longer distressing to the patient. Three grains (0.2 Gm.) in a capsule are sufficient, or even a tablespoonful of a saturated aqueous solution containing barely 4 grains (0.26 Gm.) to the ounce (30 Gm.). The first two or three doses are to be taken at intervals of half an hour or twenty minutes if necessary, and subsequently at longer intervals, according to the sensations of the patient, a limit being placed on the total number which may be taken. More than three doses is seldom required, and after the first trial one dose is often sufficient on subsequent occasions.

Chloretone also found useful in the **sickness accompanying the menstrual period** in many girls. Three sisters were every month each laid up in bed for at least a day with what might be called a bilious attack, accompanied by sickness and retching; this had gone on for some eight or ten years. After three or four months two of these girls no longer required to take chloretone at the time of the period, and the sickness ceased to occur. The third sister still took one dose of 5 grains (0.3 Gm.) each month, and had very little trouble.

In 4 cases of **seasickness** the drug proved very effective.

Chloretone gives relief of **stomach pain**. It has a pleasant taste and causes an agreeable feeling of warmth, and the slight hypnotic effect produced by 12 or 15 grains (0.8 to 1 Gm.) frequently aids the process of

relief. Hutton (Liverpool Medico-chir. Jour., Jan., 1904).

Chloretone is a valuable prophylactic against **sea- and train-sickness**, although in a few cases it does not succeed. Its anesthetic action upon the gastric mucous membrane is not sufficient to explain its effects; it probably acts as a general nerve sedative as well. Its occasional failure may be due in some instances to interference with the action of the digestive ferments. If so, this is readily avoided by taking a full dose of the drug on an empty stomach and not eating food for an hour or two afterward. John Dunlop (Lancet, March 19, 1904).

As a prophylactic for **postanesthetic vomiting** chloretone has been recommended by Hirschmann, Bowles, and Bickle. It may also be used for the relief of vomiting already established.

Chloretone given in doses of 10 to 15 grains (0.65 to 1 Gm.) half an hour before **anesthesia**, either dry on the tongue or in capsules. Sixty cases were observed, 30 receiving chloretone, the other 30 being anesthetized in the usual way. Patients who had taken chloretone required one-third to one-half less of the anesthetic than the others. None were nauseated during anesthetization and very few vomited afterward. Of the other 30 patients, 80 per cent. had nausea and vomiting. L. J. Hirschmann (N. Y. Med. Jour., Dec. 15, 1900).

Chloretone is the best drug to give **before operating**. The dosage is important. The author invariably administers 15 grains (1 Gm.) in a capsule one and a half hours before the time fixed for the operation. Sometimes the drug causes a little dizziness before the operation, the only drawback ever noted. In dental, adenoid, and tonsillotomy cases the drug is not given, as a little vomiting is useful in getting rid of swallowed blood.

The drug lessens the patient's dread of the table; the anesthetic is

taken more quietly, and very much less of it is required. The patient is very quiet in coming to. Shock is minimized in a remarkable way. Nourishment can be freely taken as soon as the patient becomes fully conscious. In operating in private houses less nursing assistance is required. L. W. Bickle (Therap. Gaz., March, 1912). S.

## CHLORIDE OF CALCIUM.

See CALCIUM.

**CHLORIDE OF ETHYL.** See ETHYL CHLORIDE.

## CHLORIDES IN THE URINE, ESTIMATION OF.—

These consist chiefly of sodium chloride, with a small amount of potassium and ammonium chlorides. The healthy adult excretes from 10 to 16 grams of chlorides in 24 hours. The chlorides are *increased* normally, by increased ingestion of salt, by abundant drinking of water, and by active exercise; abnormally, in the first few days after the crisis of acute febrile diseases, gradually increasing as the disease abates; in diabetes insipidus; in dropsy after diuresis has been established. The chlorides are *decreased* normally during repose of the body; abnormally, in all acute febrile conditions (especially when attended by serous exudations) up to the crisis, when they may disappear entirely; in pneumonia their absence always indicates a serious condition; in diarrhea; in chronic conditions with impaired digestion and dropsy; during the formation of large exudations; in acute and chronic diseases of the kidneys with albuminuria; in chronic diseases. A decided diminution or absence of chlorides in a febrile condition is strongly suggestive of pneumonia.

**Test for Chlorides.**—Place 2 drams of the urine in a test-tube, acidify with 10 or 12 drops of nitric acid, C. P., and carefully add 1 drop of silver nitrate solution (1 to 8). If the amount of chlorides be about normal, this drop will form a whitish globule, a solid white ring or one or more compact, whitish, flocculent lumps, and will settle to the bottom. If the chlorides are diminished, there will be only some cloudiness. One may use a

specimen of normal urine in another test-tube as a control. When the exact quantity of chlorides is desired, one must resort to quantitative titration, the technique of which may be found in larger treatises on Uralysis. EDITORS.

**CHLORMETHYL.** See METHYL CHLORIDE.

**CHLOROFORM.**—Although discovered during the same year by three chemists (Samuel Guthrie, of Sackett's Harbor, New York; Soubeiran, of France, and Liebig, of Germany) and Dumas gave it its present name, it was Sir James Y. Simpson, of Edinburgh, who first used it as an anesthetic in 1847.

Chloroform ( $\text{CHCl}_3$ ; specific gravity, 1.497 at 62.5° F.) is a trichloride of formyl, obtained by the action of chlorine upon alcohol, the methods usually employed being either the addition of chloral hydrate to an alkaline solution or of chlorinated lime to ethyl oxide. This is distilled and subsequently purified by the addition of sulphuric acid, sodium carbonate, and lime, and then redistilled.

Chloroform appears as a neutral, colorless fluid, possessing a sweetish and hot taste, and giving off a fragrant and characteristic odor. It possesses marked solvent powers, rapidly dissolving alkaloids, iodine, bromine, volatile oils, etc.; but it is itself only sparingly soluble (about 1 part in 200) in water. It is distinctly so, however, in alcohol, ether, benzene, and the fixed and volatile oils.

Chloroform, though volatile at low temperatures, is not inflammable under ordinary circumstances, except when mixed with alcohol. When used, however, in the presence of a gas-flame, it is likely to become decomposed into carbonyl chloride

( $\text{COCl}_2$ ), Sir Humphry Davy's phosgene, and prove noxious to persons inhaling it. Its prolonged inhalation may even cause death.

Case of a man shot in the abdomen who was brought to the hospital at night and immediately operated upon by gas-light. As a result of the chloroform narcosis, which had to be kept up for four hours, powerful chlorinated vapors were produced. Two of the surgeons and several of the Sisters of Mercy were overcome and one of the latter has since died. (*Inter. Med. Mag.*, April, 1898.)

Bronchopneumonia and edema of the lungs, with marked passive congestion of the liver and kidneys occurs also with some frequency in druggists and chemists who use chloroform in the presence of gas-flames. Kenelm Winslow (*Boston Med. and Surg. Jour.*, May 11, 1899).

In a narcosis twenty minutes long the chloroform shows evident decomposition. The higher the temperature and the brighter the room in which the narcosis takes place, the more marked is this decomposition, and, if the same portion of chloroform is twice used in the apparatus, the decomposition is still greater. E. Falk (*Deut. med. Woch.*, Nov. 27, 1902).

Research undertaken to determine the effects of administering chloroform in the near neighborhood of a gas-flame. The inquiry was suggested by the result of the installation of a gas stove in an operating theater so large as to be unduly cold. The stove was situated more than three meters from the head of the operating table. Two operations were performed under chloroform. The anæsthetist suffered from headache during the administration and afterward vomited. His two assistants also suffered from headache and a sense of illness. One of the patients, a woman of 23, who underwent laparotomy for an ovarian cyst, was made very ill. The other patient was a man aged 43 suffering from malaria and an enlarged spleen, and operated

on for inguinal hernia. He showed signs of collapse some hours after the operation and, in spite of prompt treatment, died twelve hours after operation. G. Betagh (Policlinico, Dec., 1904).

A series of experiments warranted the following conclusions: (1) The combustion of illuminating gas in a closed room, in which there is chloroform vapor, or any mixture which has chloroform for its basis, produces toxic gases which are rapidly fatal to animals, if the gases are in sufficiently large quantities. (2) The vapor causes irritation of the mucous membranes, especially that of the respiratory passages, and a very annoying cough. The condition becomes dangerous if the room is small and badly ventilated. Some individuals are more susceptible to the action of these gases than others. Grave accidents occur without warning in animals. There may be no irritative cough in the animal which is anesthetized, probably on account of the antispasmodic action of the anesthetic. The first unfavorable symptoms may be cyanosis and respiratory syncope. (3) The toxic gas in such cases is not carbonic oxide, but chloroxycarbonic acid, or phosgene. It acts upon the blood by virtue of its peculiar poisonous property, and not by being changed into hydrochloric acid and carbonic oxide. (4) Prophylaxis consists in avoiding the use of an open flame the combustion products of which are precipitated. A flame which is protected by a chimney may be used if the opening of the chimney is sufficiently large. Electricity may be used freely in the presence of chloroform, but Bunsen burners should not be used. Armand and Bertier (*Revue de chir.*, July, 1905).

Even under ordinary conditions the chloroform usually employed for anesthetic purposes tends to decompose and to form hydrochloric acid and carbonyl chloride. According to Newman and Ramsay, this latter sub-

stance is the cause of the majority of cases of after-sickness. This can be overcome by keeping a little slaked lime in the bottles and filtering the supernatant liquid as required.

Chloroform should always be pure, and this, of course, applies as well to ether; and if there is any doubt about its purity, Hepps's smelling test will enlighten one. A piece of Swedish filter paper is dipped in the chloroform and allowed to dry. If there is no odor it is pure, but if there is a peculiarly sharp, irritating odor it is not pure, and the odor is due to its at least partial decomposition into hydrochloric acid and chlorine. W. P. Burdick (*Therap. Gaz.*, June 15, 1912).

To 10 c.c. (2½ drams) of chloroform add as much benzidine as will lie on the point of a knife and shake gently, when a clear solution will form. If the specimen is pure, the solution will remain unchanged 24 hours if kept in the dark. If 0.01 per cent. of phosgene is present, it becomes cloudy at once; if 0.1 per cent. is present a yellowish-white precipitate is formed. When chlorine is present, the solution becomes pale rose in color, changing afterwards to a blue; if  $\text{HCl}$  is present, the solution becomes cloudy immediately. (*Amer. Jour. Pharm.*, Sept., 1917).

The deleterious effects of chloroform tend especially to occur when it is kept in a bottle containing air and exposed to light. It should be kept therefore in dark, preferably amber-colored, glass-stoppered, bottles, and in a cool and dark place.

There is a lack of uniformity in the standards for chloroform in the different countries—possibly due to alteration. The alcohol present acts as a preservative; 1 per cent. of alcohol is sufficient to prevent decomposition. But if the alcohol is removed and the chloroform exposed to oxygen it degenerates. Baskerville (*N. Y. Med. Jour.*, June 15, 1912).

While the actual death rate in northern climates is 1 in 2000, in warm climates it is safer, the rate being 1 in 8000. McCormick (Summit Co. Med. Soc., Akron, Feb. 1, 1916).

### PREPARATIONS AND DOSES.

—Besides being used as an anesthetic, chloroform may be administered internally or used externally. The official preparations are as follows:—

*Chloroformum* (chloroform), described above, and which (U. S. P.) should contain, by weight, 99 to 99.4 per cent. of absolute chloroform and 0.6 to 1 per cent. of alcohol. Dose, 15 to 30 minims (1 to 2 c.c.).

*Spiritus chloroformi* (spirit of chloroform), composed of chloroform 6 parts and alcohol 94 parts. Dose, 10 minims to 1 fluidram (0.6 to 4 c.c.).

*Emulsum chloroformi* (emulsion of chloroform), composed of chloroform 40 parts, expressed oil of almond 60 parts, tragacanth 10 parts, and water enough to make 1000 parts. Dose, 2 to 4 fluidrams (4 to 8 c.c.).

*Aqua chloroformi* (chloroform water), a saturated solution (about  $\frac{1}{2}$  per cent.) of chloroform in water. Dose, 2 to 4 drams (4 to 8 c.c.).

*Linimentum chloroformi* (chloroform liniment), composed of chloroform 3 parts and soap liniment (soap 66 parts, camphor 45 parts, oil of rosemary 10 parts, alcohol 725 parts, and water enough to make 1000 parts) 7 parts. Used externally.

### PHYSIOLOGICAL ACTION.—

When inhaled, chloroform is promptly absorbed through the mucous membrane of the respiratory tract. When taken by the mouth, it acts as an irritant upon the gastrointestinal mucosa, causing a sensation of heat and even burning, and impairment of the functions of the stomach, but it is never-

theless absorbed rapidly. Its fate in the body is practically unknown. What part is eliminated by the lungs, however, appears to be unchanged.

**Nervous System.**—The anesthetic effect of chloroform is at present believed—though on rather weak grounds—to be due to a dissolving action on fats, particularly those of the nerve-cells. This would disturb their metabolism and thus temporarily inhibit their functional activity. The predilection of chloroform for fats is ascribed to the fact that it is more soluble in these bodies than in other fluids, especially water, the organism contains. As a result of this action on the nerve-cells, there would occur a brief period of stimulation, recalling, as far as the action on the cerebrum is concerned, that observed in alcoholic delirium. This would soon be followed by the marked depression which initiates the period of surgical anesthesia.

After chloroform anesthesia there is severe dilatation or atony of the vessels which is pronounced and long continued. This morbid vascular reaction is sometimes manifest from 1 to 6 weeks after operation. This phenomenon is explained by the fact that the central vasomotor mechanism is extremely sensitive to injurious influences brought to it by the blood. Alternate **hot** and **cold douches** seem, however, to restore it. E. Weber (Med. Klinik, xi, 991, 1915).

As chloroform yields free hydrochloric acid when inhaled, the writer deems it possible that this action contributes materially to the toxic effects. Experiments in animals showed that **sodium carbonate** added to hypertonie **saline solution** inhibited in part the toxic phenomena. These were also less marked in animals which had received the alkali prior to the use of chloroform. E. A. Graham (Arch. Int. Med., June, 1920).

Chloroform acts successively upon the cerebrum, cerebellum, the sensory and then the motor side of the spinal cord and medulla, causing one after another: sleep, loss of sensibility, loss of reflexes, muscular relaxation, and finally respiratory and vasomotor paralysis. This action is similar to that produced by ether, but three times the quantity of the latter is necessary to produce corresponding effects.

*Circulation.*—Chloroform acts distinctly as a circulatory depressant. It has been shown to depress the heart about eight times as strongly as ether. The circulatory depression is not due, however, as much to a direct action on the heart itself by the chloroform present in the blood as to one on the vasomotor system through a direct action on the vasomotor center and the vessel walls. The vasodilation produced during the stage of narcosis affects particularly the vessels of splanchnic area, the blood accumulating in the central vascular trunks of the body. Hence the fact that the skin is pale. A gradual fall of the blood-pressure also occurs, owing to the vasodilation, and because of the heart depression the latter causes. On the whole, death from chloroform is mainly and primarily due to vasomotor depression.

The circulation may, however, be affected in a different way. Thus a few whiffs of chloroform have sufficed in some cases to produce death. This has been ascribed to irritation of the nasal mucous membrane, which, in turn, gives rise, through the branches of the fifth pair it contains, to reflex inhibition of the heart by way of the vagus, Dogiel having

found that it did not occur when the vagi were cut. To avoid this untoward effect in practice, where it is not infrequent, the application of a solution of cocaine to the nasal mucosa to dull its sensibility has been used with success in some instances.

*Respiration.*—The respiratory center may be depressed reflexly during the first stage, by irritation of the terminals of the vagus in the upper respiratory tract. The respiratory movements may thus be slowed or even stopped very soon after the use of the anesthetic is begun, but this danger—which may also be counteracted in a measure by spraying the nasal cavity with a 5 per cent. solution of cocaine—is of short duration.

During the second stage respiration may be interfered with by struggling, during which the patient alternately holds his breath and takes deep inspirations or, rather, resorts to deep gasping movements.

Chloroform also tends to depress the respiratory center directly, but this becomes manifest only during the third stage of narcosis, when the respiration becomes slow and shallow. When the anesthetic is pushed respiratory arrest is further favored by circulatory failure, the lungs, like all other peripheral organs, being, so to say, exsanguinated by the accumulation of the blood in the great trunks of the abdominal cavity.

Death during light anesthesia produced experimentally in 18 cats. Fibrillation of the ventricle followed by cardiac arrest was always found to be the immediate cause of death. The animals were but partially anesthetized. Levy (Proceed. of the Physiol. Soc., Jan. 21 and Oct. 21, 1911).

There is increased slowness and weakness of the respiratory move-

ments until these are caused to cease by paralysis of the center.

Plethysmographic experiments in cats show clearly that the initial effect of chloroform is to produce a marked diminution in the average depth and generally a slight increase in the frequency of respiration. Subsequently the depth of respiration becomes constant at a lower level. The cessation of respiration, which is an initial danger point in chloroform anesthesia, and may result in death, is the direct effect of deep and rapid respiration prior to anesthesia, and the higher the percentage of the drug administered, the more likely it is to occur. This can be rendered negligible by a low percentage of chloroform, though the writers believe that some trace of an initial danger point is rarely absent. They ascribe the cessation of breathing on administration of chloroform after deep and rapid respiration to the diminished carbon-dioxide content of the blood which the latter entails, the chemical stimulus necessary to keep the respiratory center in activity being thereby reduced. The effect of the anesthetic would be, in addition, to reduce the excitability of the center to carbon dioxide, so that the quantity of this gas, even after a minute or two of reduced respiration consequent on the administration of the drug, would not be sufficient to maintain respiration, which would accordingly cease. In support of this hypothesis the authors present experiments showing that with a deep and rapid respiration the carbon-dioxide content of the blood is much less than with normal lung ventilation. Animals allowed to recover partially from chloroform (to the point when reflexes are well marked and voluntary movements begin), but with their lung ventilation still at a low level, show apparently an increased tolerance to the drug, the initial effects on the respiration, upon resuming the chloroform, being much less marked, even with very high

percentages of the drug, than at the first induction of anesthesia.

The view having recently been expressed that during chloroform narcosis the blood retains unimpaired up to the time of death its normal capacity of absorbing oxygen, and that if the amount of this gas diminishes in the blood the decrease is solely due to the slowing of the respiration, the authors undertook to settle this point definitely. Upon measuring the gas content of the blood before and during anesthesia they found the fall in oxygen content during the second stage of anesthesia to be about 40 per cent., and in the initial stages often even greater than this. The hemoglobin is thus only partly saturated with oxygen during narcosis, the amount present indicating an oxygen tension in the blood of 45.5 mm., as compared with 99.49 mm. in the normal cat. Further experimentation showed that during narcosis diminished respiration alone does not reduce to any noteworthy extent the oxygen content of the blood. The authors therefore conclude that the diminution of oxygen content is not mainly due to diminished respiration, but to the action of the drug on the red corpuscles. They had already demonstrated and recorded the fact that as much as 97 per cent. of the chloroform in the blood may be associated with the red cells. Buckmaster and Gardner (New York Med. Jour., from Proceedings of the Royal Society, Dec. 28, 1911).

The work of Brodie and Widdows and Buckmaster and Gardner shows that the absorption of chloroform increases with great rapidity in the initial stages of anesthesia to a value which approaches a maximum. Brodie and Widdows show that the period of maximum absorption is during the second minute of the administration, but Buckmaster and Gardner place the time somewhat later, from five to fifteen minutes in three instances.

Following this maximum of absorp-



tion the breathing becomes shallower, probably owing to the effect of the chloroform on the respiratory centers. This depression of respiration varies in different individuals, and appears to depend on the degree of concentration of the chloroform-air mixture. During the period of respiratory depression the rate of absorption diminishes.

At this stage in animals the author found that there was danger of the respiration completely stopping, and that, although artificial respiration was frequently successful in restoring the breathing, this was not always the case. G. Herbert Clark (Glasgow Med. Jour., July, 1912).

**Blood.**—The widespread influence of chloroform is accounted for by the fact that it is taken up from the pulmonary alveoli by the red corpuscles, which serve to carry it to all tissues. The power of the blood to take up oxygen is also reduced.

After the inhalation of chloroform the glycogen in the liver decreases, while the reducing power of the blood increases. The action of chloroform upon the blood *in vitro* confirmed the results obtained *in vivo*. Under these conditions hydrolysis of the glucose occurs, with the formation of the fermentable sugar belonging to the hexose group. Garnier (Revue méd. de l'est, No. 8, 1901).

The writer's researches on the physical relation of chloroform to blood showed that the absorption of chloroform vapor is greater by blood than by saline solution, and that blood acts as a special carrier of chloroform to the tissues just as it acts as oxygen carrier. The combination which certainly takes place between chloroform and protoplasm may possibly be accounted for on the lipid theory (the union of chloroform and "lipoids"). The question whether chloroform can combine with all protoplasm indifferently, or with its fatty constituents (lecithin,

cholesterin) more particularly, is a subsidiary issue, in respect of which the above observations contain no decisive evidence. On the other hand, all protoplasm is subject to the influence of chloroform, while, moreover, all protoplasm is associated with fatty constituents of which lecithin is the most universal representative. Lecithin is widely distributed in vegetable as well as in animal protoplasm; it is present in blood-serum, which, as shown by Moore and Roaf, has a solvent power toward chloroform not far short of that possessed by blood. A. D. Waller (Proc. Royal Soc., July 19, 1904).

**Elimination.**—Cessation of the administration of chloroform by inhalation is followed by the elimination of a considerable proportion of the amount absorbed—at least one-half—during the first twenty-five minutes. Nicloux found that the same proportion was eliminated in five minutes in dogs. The case is different when the drug is given either by the mouth or hypodermically. Absorption is much slower,—the maximal amount in the blood not being reached, according to Clark, until about four hours after administration by the stomach, and not until about five hours after injection. The tissues are thus exposed much longer than when the drug is used as an anesthetic. This has an important bearing upon the after-effects of chloroform.

Series of experiments on rabbits to determine the relative distribution of chloroform in the red cells and the plasma when given by inhalation and when administered subcutaneously. By inhalation the plasma acquires from 9.2 to 14.8 per cent. of the total amount found in the blood; by injection from 18.4 to 27.6 per cent. is found in the plasma. The authors believe that, inasmuch as the drug is

promptly given up by the red cells and long held in the plasma, the presence in the latter of an excess of the chloroform over that usually found is the cause of the development of delayed chloroform poisoning. Their experiments serve to confirm this view, for one animal which died just prior to the cessation of chloroform inhalation was found to have 32.3 per cent. of the drug in the plasma. The delayed elimination of the drug from the plasma allows it to continue to act detrimentally upon the liver and kidneys. These organs were found to be more severely damaged in the animals receiving the drug subcutaneously than in those which were allowed to inhale it. Clark and Lindsay (*Lancet*, July 27, 1912).

**Metabolism.**—This process is but slightly influenced by chloroform when it is inhaled. There is a slight stimulation of hepatic metabolism, as shown by an increased conversion of ammonia into urea (Noël Paton). When the use of chloroform as an anesthetic is prolonged or repeated at short intervals, say three or four days, or when it is given repeatedly by the mouth or hypodermically, it tends to irritate the kidneys, the urine showing granular casts and renal epithelium. Hence the fact that the quantity of urine voided, while normal or increased at first, may become scanty after a too free use of the drug. Albuminuria, acetonuria, and urobilinuria have been noted. The amount of urine secreted is sometimes greatly increased, however, soon after the anesthetic is stopped.

Series of experiments on rabbits to ascertain the effect of chloroform upon normal kidneys and upon these organs after injury. Narcosis prolonged for two hours always proved fatal either directly or after a few days. Autopsy showed marked fatty

degeneration in the kidneys, liver, and heart. A series of experiments in which rabbits were killed at various intervals after a few minutes' narcosis showed that the fatty changes in these organs disappeared in about eight days. Pregnancy *per se* had no effect on these changes, but the hearts of the fetuses showed fatty change. If the renal artery on one side was tied, this organ showed no degeneration. If both veins or ureters were ligated, or any of the renal poisons given before narcosis, the effect was much increased.

If chloroform was given for a few minutes one day and after a few days again administered, the second narcosis always proved fatal. Chemical examination showed that the fat content of the liver was increased and that of all other parts lessened after narcosis. The writer believes that the injury to the kidney causes a nephrolysis, which itself causes death after several days. Offergeld (*Arch. f. klin. Chir.*, Bd. lxxv, S. 758, 1905).

While the normal percentage of sugar in the blood of rabbits was estimated at 0.12 or 0.14 per cent., it was found to be increased to 0.3 or 0.4 per cent. during chloroform narcosis. A few hours after, however, it was found to be reduced to 0.03, 0.04, 0.05, and 0.09 per cent. This suggests that an increased consumption of carbohydrates takes place within a short time. It is only after the expiration of twelve hours that normal conditions are resumed.

That the changes are not the result of retarded combustion of carbohydrates induced by chloroform poisoning is shown by the fact that, despite the high percentage of sugar in the blood, grape-sugar is seldom found in the urine. J. Arnheim (*Wiener klin.-therap. Wochen.*, Oct., 1905).

The writer found urobilin constantly in the urine in the 25 children examined before and after general anesthesia with chloroform. The amount was proportional to the dura-

tion of the anesthesia. He thinks that it was evidently due to destruction of red corpuscles by the drug, the passage of hemoglobin through the kidneys, and its transformation into urobilin. Gianasso (*Riforma Medica*, vol. xxii, No. 20, 1906).

Chloroform narcosis influences renal activity as follows: 1. In the early stages, when the anesthesia is light, the quantity is frequently increased. During free anesthesia the secretion is always diminished, and may be suppressed. 2. The after-effect is always a great increase. 3. The total excretion of nitrogen is greatly reduced. 4. The urine secreted during chloroform anesthesia contains less nitrogen than the normal urine. Hence chloroform affects not only the blood-flow through the glomerulus, but also the secretion of nitrogenous solids into the tubules. 5. In prolonged narcosis, with marked diminution of urine volume, there is a considerable exudation into the renal tubules of leucocytes which subsequently escape with the urine. 6. The excretion of chlorides is much increased both during and after chloroform narcosis. 7. Albumin appears in a small proportion of experiments after chloroform inhalation. 8. Reducing substances other than glucose are almost invariably increased. W. H. Thompson (*Brit. Med. and Surg. Jour.*, March 17, 1906).

**CHLOROFORM AS AN ANESTHETIC.**—The merits of chloroform are, as a rule, compared with those of ether. Its advantages over the latter, however, taken collectively, are not such as to render it the anesthetic of choice; ether has won this position in the United States, the continent of Europe, and the south of England, while India, tropical countries, and Scotland still prefer chloroform. In this country, however, no physician is safe before the law-courts, unless

he gives chloroform only when ether is contraindicated.

Advances in general and local anesthesia in the past few years have been as great as in any branch of medicine. Local anesthesia now suffices for many minor and major operations, a weak solution of cocaine, with one or more adjuvants, being entirely efficient. Spinal anesthesia has undergone improvements and is satisfactory for operations on the legs and lower portion of the abdomen. General anesthesia, following hypodermic injection of morphine and hyoscine, requires very little of the anesthetic. In some conditions, especially in obstetrics, the hypodermic injection takes the place of the inhalation anesthetic. New drugs have been proposed for inhalation anesthesia. Ether and chloroform are still supreme, however, notwithstanding their disadvantages. Abbe (*Amer. Jour. of Obstet.*, April, 1908).

In favor of chloroform are the following facts: it acts more rapidly than ether and is more pleasant to the patient; it is less pungent than ether and tends less to irritate the respiratory tract; the preliminary excitement is less marked and the patient is anesthetized more rapidly; it does not excite a flow of mucus and saliva to the same degree; vomiting occurs less frequently, though when it appears it is more prolonged; it is practically non-inflammable; it does not give rise to a condition akin to that known as "ether pneumonia"; the rapidity with which it produces anesthesia is advantageous when many patients, as is the case with wounded soldiers after a battle, must undergo operations.

Chloroform is also deemed preferable to ether under the following conditions: When rapid anesthesia is

desired; in patients who have bronchitis or emphysema, to avoid the irritation of the tract caused by ether; in operations in the nose, nasopharynx, pharynx, trachea, and mouth, because the greater activity of chloroform renders the maintenance of the anesthesia easier, while necessitating less interference with the surgeon's work and causing a much less copious flow of mucus; in brain surgery, to avoid the meningeal congestion produced by the vomiting due to ether; in cases in which there exist vascular degenerative changes, such as atheroma and aneurism, and where the rise of blood-pressure produced by ether would tend to produce vascular rupture; in tropical climates, where ether is too volatile and chloroform appears to be safer than ether; where the operation has to be performed by artificial light other than electric lamps—excepting those in which, as in the arc light, the flame is exposed to the air—and where the actual cautery is to be used, ether readily catching fire and having caused injury when these precautions were not taken. Under all other conditions, ether should be given preference even though its likelihood of causing respiratory complications is greater.

Out of some 2400 patients who were etherized, 10 developed temperatures with some respiratory complications, 6 of these having bronchitis, 1 pleurisy, and 3 bronchopneumonia, 1 of the latter being fatal. Seven of these cases occurred in the summer. In none of the 10 cases had there been a previous history of bronchitis; all were in good condition and took the anesthetic well. The operations were prolonged ones, and with 1 exception on the trunk, necessitating bandaging, which would prevent free expectoration. A number of pa-

tients in bad condition from alcohol or sepsis, and subjected to short operations under ether, developed no lung complication. Conversely, not 1 out of 600 chloroform cases, of which many were for mouth operations, developed any respiratory trouble. Crouch and Corner (*Lancet*, May 24, 1902).

While, for general work, ether is approximately five times as safe as chloroform, there are still some conditions for which chloroform is recommended on account of its special properties. These are: (1) in the treatment of certain convulsive seizures; (2) in obstetric practice; (3) in the presence of kidney lesions; (4) in elderly persons with dyspnea; (5) in operations on the brain it is preferred by some surgeons; (6) in obstructed conditions of the trachea, esophagus, and larynx; (7) in deep cellulitis of the neck. It is to be particularly avoided (1) in all conditions of heart weakness; (2) in all operations requiring the semirecumbent or sitting posture, particularly in dental operations; (3) in minor surgical operations. The cause of fatal accidents in chloroform anesthesia has been shown to be overdosage, a direct poisoning of the heart by blood overloaded with chloroform. This happens even in the beginning of the anesthesia, when the actual amount inhaled has been small; a sudden deep inspiration carries a densely concentrated vapor to the lungs and blood loaded with chloroform enters the coronary arteries and paralyzes the heart muscle. W. D. Haggard (*Jour. Amer. Med. Assoc.*, Nov. 7, 1908).

The statistics usually given vary in showing ether to be from two to seven times as safe as chloroform, averaging about four times. These figures, however, are based wholly on records of deaths during the administration or directly thereafter; they take absolutely no account of the ultimate restoration of the patient to sound health, and the writer wishes to inquire, "What is a man profited

if he gain a 'successful operation' and die six months later of consumption?" It has seemed to him that the figures given express the relative safety of the surgeon's reputation, and the ultimate safety of the patient is in nearly inverse ratio. The writer recommends that every candidate for anesthesia be examined thoroughly for evidences of cardiac, renal, or pulmonary fault; that the omnipresence of tuberculosis be borne in mind, that the patient be given the benefit of the doubt, and, finally, that, except with the most positive contraindications, chloroform be used. R. S. Hart (Journal-Lancet, Oct. 1, 1912).

**Contraindications.**—*Respiratory Disorders.*—Disorders of the respiratory tract in which interference with the movement of the air prevails, stand out prominently in this connection. Great caution should be observed in the administration of chloroform in all asphyxial conditions,—i.e., when the respiratory area is to any degree restricted through the presence of growths, inflammatory lesions, emphysema, etc. In lymphatic and tuberculous children the presence of enlarged bronchial glands is to be surmised, and the anesthetic should be administered with unusual care. An enlarged thymus greatly increases the likelihood of untoward effects.

Autopsy in the case of death from chloroform in a boy of 14 years showed a persistent hyperplastic thymus gland, hypertrophy of the lingual tonsil, and marked enlargement of the spleen. As these phenomena have been observed in numerous instances by other observers, the author believes that their presence in children may be taken as a safe contraindication to chloroform administration; the mediastinal and oropharyngeal glands likewise. L. Laqueur (Deut. med. Woch., Feb. 13, 1902).

General anesthesia with chloroform seems to have a decidedly un-

favorable action on incipient tuberculosis whipping it up to a more rapid course, as observed by the writer in 3 typical instances. Suspicion of tuberculosis should warn against the use of chloroform on account of its depressant action on the liver, etc. If chloroform has to be used, as little as possible should be given and for the shortest time possible. Olivares (Revista Medica, Pueblo, Mex., Dec. 15, 1918).

In affections complicated by liquid effusions, however, the danger may be thwarted when it presents itself, as shown by Guermonprez, by evacuation of the pleural contents. He saved a case in *articulo mortis* from chloroform anesthesia by promptly removing pus from the pleural cavity.

There is no antidote to chloroform. Fatalities have occurred when morphine, atropomorphine, chloral, and other antecedents have been administered. Chloroform is contraindicated in emphysema, acute and chronic bronchitis, and, above all, in severe septicemia; in the latter disease chloroform quickly causes fatal complications: sudden death by syncope or postoperative collapse. Laryngeal affections complicate anesthesia. The writer met with spasmodic glottic crises in 1 of his cases. Pleural adhesions are often associated with accidents. In 10 deaths under chloroform, 7 showed pleural adhesions. Mauclair (La Médecine moderne, Nov. 18, 1902).

The necessity of keeping the respiratory tract clear of all obstruction extends to the period of anesthesia itself, when saliva, mucus, blood, etc., may accumulate in the larynx, trachea, and bronchi without giving rise to early danger signals. This danger may be averted in part by tilting the head to the side where possible. Falling back of the tongue, by preventing the access of air to the lungs; foreign bodies, such as false

teeth, vomited matter, etc., are to be guarded against. Sufferers from bronchitis, especially children, stand either badly, however; in such, chloroform is preferable.

Practice will alone make an expert anesthetist for children. The drop method is best, and the dose should be gradually diminished as insensibility begins. Color and rate of respiration are the indices of safety. The tongue is liable to fall into the pharynx. In case of collapse, artificial respiration is demanded, rhythmic traction of the tongue not being sufficient. Savariaud (*Jour. de méd. de Paris*, Aug. 10, 1912).

*Cardiac and Circulatory Disorders.*—

On the whole, chloroform anesthesia does not seem to cause untoward effects in the average case of heart disease, unless feeble heart action, dyspnea of cardiac origin, arrhythmia, or an acute disease of endocardium, myocardium, or pericardium be present. Fatty degeneration and dilatation are contraindications mainly because of the danger of reflex inhibition during the first stage of anesthesia, the myocardium being less able to oppose the inhibitory impulses received through the vagus.

Valvular lesions only increase the danger if they are obstructive. In that case, even, compensative hypertrophy may also compensate for the extra resistance induced.

Physicians and surgeons are agreed that accidents in chloroform anesthesia are not more frequent in patients with aortic or heart disease than in patients with other illness. Nor does cardiac or aortic disease contraindicate chloroform as an anesthetic, if the disease is not acute and infectious, if the patient is not too feeble, or if dyspnea, asystole, or symptoms of pericardial symphysis have not appeared. In some cases of

atheroma and cardiac disease the heart condition is even improved after chloroformization. The main contraindication to chloroform in patients with heart disease is the presence of dyspnea. This is, however, but temporary. Accidents may be due to impure chloroform, or may occur under chloroform, and yet not be due to it. Huchard (*Jour. des praticiens*, May 31, 1902).

Series of 6000 chloroform anesthetics with but 3 deaths. One, a man of 23 with a previous history of alcoholism, died during operation, his heart suddenly ceasing to beat in diastole. Nothing could resuscitate him. Autopsy showed a very fatty heart, the ventricular walls being one-half fat. This was probably the result of excessive alcohol. Chloroform is, therefore, contraindicated in cases of fatty degeneration of the heart. Barette (*Jour. des praticiens*, March 1, 1902).

The writer has often observed that chloroform is well tolerated by individuals affected with valvular heart disease, angina, and atheroma. He is inclined to consider chloroform as a comparatively safe anesthetic in these cases, excepting only those suffering from fatty cardiac degeneration. But due caution in administering the anesthetic is imperative. Respiration and pulse should be watched unceasingly, and the drug given in small quantities.

Brouardel, in autopsies on 25 cases of death from chloroform, found no valvular heart disease in any of them. In 4 fatty degeneration or fat accumulation about the cardiac muscle was recorded. Most of the fatal cases died suddenly, before the operation was begun, from cardiopulmonary syncope. Guyon (*Semaine méd.*, vol. xxii, No. 9, 1902).

In arteriosclerosis and aneurism the main danger lies in the struggling of the patient, since it tends to counteract the lowering of the blood-pressure chloroform produces, and to bring on

an elevated vascular tension which exposes the diseased vessels to rupture. It is not contraindicated, therefore, in uncomplicated cases, *i.e.*, where there are no pulmonary disorders in which dyspnea is a symptom. Advanced cases, owing to the rigidity of their arteries and the obstruction they offer to the circulation, especially in the coronaries, do not bear chloroform anesthesia as well, being liable to cardiac collapse.

Chloroform anesthesia is not necessarily contraindicated in cases of pronounced arteriosclerosis. In the writer's cases, apoplectic symptoms have been observed in arteriosclerotic subjects under the influence of chloroform, but they are extremely rare, and he ascribes them more to the excitement than to the arteriosclerosis. A history of attacks of angina pectoris did not add to the gravity of the general anesthesia. Even patients with myocarditic changes in the heart-muscle tolerate the chloroform well, provided the heart affection is well compensated, the kidneys still acting well, and there is no bronchitis or emphysema. The combination of arteriosclerosis with emphysema and bronchitis renders the prognosis much graver. On the other hand, arteriosclerosis in younger patients is liable to produce some very disastrous surprises. Examination of the heart and kidneys reveals nothing abnormal, but there is likely to be serious collapse under the influence of the anesthetic, and the rigid, tortuous course of the peripheral arteries is then noticed. The patients are usually revived in these cases, but the writer has encountered instances in which the patient succumbed to heart-failure six or seven hours later.

The writer is of the impression that an arteriosclerotic individual bears better a deep than a superficial anesthesia. The persisting reflexes may affect the heart injuri-

ously. Such persons tolerate the anesthesia better than the pain. E. Siegel (*Münch. med. Woch.*, Bd. viii, Nu. 13, 1906).

Preliminary treatment of any morbid process that may be present is helpful in preventing complications during anesthesia.

*Diseases of the Liver.*—Ungar found over twenty-five years ago that chloroform, when anesthesia was prolonged or repeated, gave rise to fatty degeneration of the liver. Strassman and Offergeld then showed that the hepatic lesions were more severe when loss of blood, as occurs in the course of operations, weakened the subject anesthetized. As we shall see under Delayed Chloroform Poisoning, the latter is apt to manifest itself from six hours to six days after the operation, when in many instances all danger is thought to have disappeared. The liver loses the power of carrying on its functions as a detoxicating organ and of fulfilling its rôle in metabolism; a general toxemia then ensues, which generally ends in death. The hepatic lesions have been compared to those of acute yellow atrophy; but they seem to be distinct in many particulars. This indicates the need of limiting as much as possible the length of the anesthesia whenever any hepatic disease, especially cirrhosis or yellow atrophy, is present.

Chloroform poisoning, in common with a number of closely related conditions characterized by intoxication and marked changes in the liver (acute yellow atrophy, phosphorus poisoning, certain septicemias, and some cases of puerperal eclampsia), probably all depend on the effect on the liver of poisons that destroy the synthetic functions of the liver-cells without destroying their autolytic

ferment. Autolysis of the liver-cells follows, with resulting alterations in the liver structure, and the appearance of products of autolysis (amido-acids and various other organic acids) in the blood and urine. It is probable that in chloroform and in phosphorus poisoning, at least, it is the oxidizing enzymes that are particularly involved, accounting for the marked fatty changes that are present in these conditions. II. Gideon Wells (Jour. Amer. Med. Assoc., Feb. 3, 1906).

A series of personal experiments have shown beyond doubt that chloroform is a powerful poison, that narcosis with this drug for any considerable length of time invariably causes central necrosis of the liver (in animals), and that this necrosis, if extreme, will cause death. The essential change is an extensive necrosis and fatty degeneration of the liver. There may be numerous ecchymoses and hemorrhages into the peritoneum or upper intestinal tract. The pancreas may show many fat necroses and ecchymoses. The kidney and heart may present a moderate grade of fatty degeneration. Repair is effected by solution of the necrotic liver-cells and rapid multiplication of the remaining peripheral cells. Cirrhosis does not follow extensive central necrosis and repair. Whipple and Sperry (Johns Hopk. Hosp. Bulletin, Sept., 1909).

*Renal Disorders.*—As will be shown under Delayed Poisoning, chloroform tends, when administered internally even in small doses and during prolonged anesthesia, to produce fatty changes and cellular necrosis in the kidney, the urine showing granular casts, albumin, acetone, and other evidences of serious renal involvement. It follows that the presence of any renal disease should at least counsel prudence, and if chloroform is used at all—ether is as harmful in this connection—a short period of

anesthesia. In 56 cases studied by Friedländer 44 showed nuclealbumin in the urine; 80 per cent. showed albumin, and 60 per cent. hyaline and sometimes granular casts, in Ajello's 214 cases. It is evident that under these conditions the use of chloroform is contraindicated when the kidneys are diseased to any serious extent. Yet if any operation is required in a case of Bright's, the small quantity of chloroform required as compared to ether renders the former the safer of the two. As small a quantity as possible should be administered.

Permeability of the kidneys after chloroform narcosis tested with solution of rosaniline. As a rule, it took twenty-four hours to get rid of all traces of the pigment, the patient having, as far as was known, healthy kidneys. In every case elimination was delayed by chloroform anesthesia; while it took thirty-five hours to eliminate the pigment before chloroform, in 1 case it required forty-one hours afterward. No constant relation between the quantity of chloroform and duration of the anesthesia and the alteration in renal function could be detected, as the personal equation of the kidney varies so much. The quantity of urine after chloroform narcosis was, for the most part, reduced. Benassi (Gazz. degli Osped., March 3, 1901).

If pieces of kidneys taken from an animal that died from chloroform are hardened and fixed by proper reagents, the border of the epithelial cells in the convoluted tubes is destroyed. This is of extreme importance, as the border of the epithelial cells is to the kidney what the rods and cones are to the eye, which being destroyed will render the eye blind. The kidney, therefore, losing that border, can no more serve as a filter. The integrity of the epithelial cells is absolutely indispensable for a good function of the organ. We know now that the function of the cells



with their intact border is secretion. They extract from the blood certain products. The renal secretion will therefore depend upon the integrity of the cells of the tubules. This important function is impaired by chloroform, when administered as an anesthetic, but the cell is capable of recuperating. Renaut (*Jour. des praticiens*, No. 15, 1902).

**DELAYED CHLOROFORM POISONING.**—This additional morbid effect of chloroform is considered early in this article because its pathology elucidates materially the toxicology of the drug, a fact which in itself tends to suggest prophylactic measures.

Its occurrence is all the more distressing in that it develops with comparative suddenness when the patient has passed safely through the period of anesthesia, *i.e.*, from one-half to six days after the operation. Cerebral symptoms are usually the first to appear; the patient becomes dazed, irritable, and restless, and soon shows fright, accompanied by shrieks, moaning, grinding of teeth, struggling, and even delirium. This period is followed by one of apathy attended by marked nausea and vomiting, often of coffee-ground matter. A waxy hue of the skin is soon replaced by icterus, which becomes generalized and deeper in color. Though pain is generally absent, the patient may complain of one located in the shoulder and right chest,—the typical hepatic pain,—and also of sensitiveness of the liver and gall-bladder on pressure. The mucous membranes are often deep red, owing to capillary engorgement, while the skin may show hemorrhagic areas.

The pulse is usually rapid and of low tension and subsequently irregu-

lar; the temperature may even be subnormal except when the patient is *in extremis*, when it usually becomes elevated, reaching at times 106° F. Dyspnea, Cheyne-Stokes respiration, and cyanosis are frequently observed. The pupils are dilated, fixedly so in advanced cases. The breath may be exceedingly fetid or sweetish, denoting acetone, which is usually found in the urine with diacetic acid and albumin. The case then lapses into stupor, sometimes attended with convulsive seizures, and death follows in from two to five days after the operation.

Chloroform is apt to produce fatal after-results in children who suffer from a peculiar condition of fatty liver. The writer first advanced this view nine years ago, but it was not generally accepted; the cause of death in his cases was attributed to carbolic acid poisoning or fat embolism, rather than to chloroform. In this article he reports a further series of 4 cases, all of which came to autopsy, and which seem to prove the following points: (1) That neither carbolic acid nor fat embolism plays any part. (2) That the severity of the operation cuts no figure. (3) That the only pathological condition commonly found *post mortem* is an intense fatty degeneration of the liver. (4) That the only other common circumstance was the administration of chloroform. It seems probable that in these cases the liver, being previously to the operations in an advanced stage of fattiness, was on the verge of functional inadequacy. Chloroform, by decreasing the already deficient oxidation, aggravated the condition of fattiness, and so lowered the hepatic functions that ptomaines or toxins escaped into the general circulation. Further, it prevented the elimination of these poisons by the urine. Guthrie (*Lancet*, July 4, 1903).

Case of a girl aged 3 years who underwent an operation for excision of the upper ends of the radius and ulna. Chloroform was given for thirty minutes, 5 drams of pure chloroform being used. During the afternoon the child vomited, had a bad night, and was very restless all the next day, complaining greatly of thirst. Late in the day she vomited considerable coffee-ground material, and died the next morning, forty-two hours after the operation. Autopsy showed that death was not due to fat embolism, chemical agents, or septic poisoning, but that the case was probably one of delayed chloroform poisoning. The main symptom in most cases is retching and vomiting. Carmichael and Beattie (*Lancet*, Aug. 12, 1905).

The writers have encountered a series of fatalities after operations for appendicitis which they ascribe to the injurious action of chloroform on the liver. The disturbances developed on the first or second day after the operation, the patients showing signs of extreme and progressive weakness, sometimes accompanied by jaundice and blackish vomiting. The patients all succumbed in two or three days, and extremely severe lesions were discovered in the liver in every instance. The lesions of peritonitis could never cause such fulminating toxic accidents, and there were no signs of inflammation of the liver—merely a total cellular necrosis with the aspect observed in pernicious jaundice. Weill and Vignard (*Lyon Chir.*, Dec., 1908).

In a personal case and 40 found in the literature, the writer noted that in nearly all instances marked interference with the systemic blood-current was brought about by the surgical procedure, and believes that certain toxins were thus produced which had a special injurious action on the hepatic parenchyma. His own case was that of a young woman, seemingly healthy, save for some tendency to chlorosis, who inhaled about 60

Gm. (2 ounces) of chloroform given by a skilled anesthetist. No other anesthetic was combined with the chloroform. All went well until the following day, when the patient became restless, vomited, and showed the evidences of circulatory disturbance by a soft, rapid pulse. The abdomen was flat and not sensitive, save in the liver region, where some tenderness was elicited. The eyes were slightly jaundiced. There was much albumin in the urine, and the patient manifested the stupor of eclampsia. Vomiting, jaundice, and failing heart became more pronounced, and the woman died within sixty-eight hours after the abdominal section. Autopsy showed marked fatty degeneration of the liver, without peritonitis or other evidences of inflammation or of infection at the site of operation. A. Sippel (*Archiv f. Gynäk.*, Bd. lxxxviii, Nu. 1, p. 167, 1909).

Case of jaundice due to chloroform. A man 24 years of age suffering from lead intoxication, and in addition addicted to alcohol, came under treatment for a fractured patella with contusion of the adjoining soft parts. Under chloroform anesthesia, which proved rather difficult of administration, the three fragments of bone were brought together and fixed by the loop method. Persistent vomiting followed the operation, and for several days the patient presented a slight icteric hue, without any particular elevation of temperature, but with the pulse at 110. The jaundice then progressively deepened; anuria, delirium, and stertorous breathing appeared, and death followed after a brief period. The autopsy revealed enlargement of the spleen, kidneys, and liver. Sieur (*Bull. médical*, May 14, 1910).

Fat administered to animals, and presumably stored in part in the liver, increases its susceptibility to the injurious action of chloroform. The liver cell fat evidently determines the fixation of chloroform and occurrence of necrosis. Carbohydrates, as also found by others, protect the body

proteins from disintegration. Opie and Alford (*Jour. Amer. Med. Assoc.*, Mar. 21, 1914).

The phenomena of late poisonings, edema, multiple hemorrhages, fat infiltration and necrosis are due to acids and to the fact that the amount of acid formed parallels the chemical dissociability of the drug outside of the body. Its main features are produced merely by the administration of hydrochloric acid, while the areas of central necrosis in the liver caused by various substances give an acid reaction to neutral red. Sodium carbonate in a hypertonic sodium chloride solution markedly inhibits the production of the lesions. The halogen acid (hydrochloric, hydrobromic or hydriodic acid), directly liberated in the process of dissociation, may be the pathogenic factor. E. A. Graham (*Jour. of Exper. Med.*, July, 1915).

Delayed chloroform poisoning is met with in children with relative frequency. The symptomatology does not differ from that observed in adults.

Three cases of delayed chloroform poisoning in children which terminated fatally" fifty, thirty-eight, and thirty hours, respectively, after operation. In 1 of the cases the writer was informed that 2 other children of the same family had died in much the same way, but without any anesthetic having been given. In another of the series a brother of the patient had died in exactly the same way the day after being operated on. Campbell (*Med. Press and Circular*, Feb. 20, 1907).

Fatal case of delayed chloroform poisoning or acid intoxication occurring in a boy aged 3 years and 10 months. The child was operated upon for phimosis and was given chloroform for seven minutes, about 2 drams (8 Gm.) being used. Thirteen hours later symptoms of acid intoxication set in, and the child died about twenty-four hours later. No antiseptics were used such as might contribute to the cause of death.

Telford reports 3 cases, 2 in boys aged  $2\frac{1}{2}$  and  $1\frac{3}{4}$  years, respectively, and in a girl aged 8 years. The operations were for tuberculous epididymitis, right inguinal hernia, and double genu valgum. The younger boy recovered. We do not seem any nearer to a solution of these cases—why certain children will develop a state of acid intoxication after the administration of an anesthetic and die with fatty degeneration of the liver, kidneys, and heart. The condition is not rare, as the writer has seen 4 deaths out of 1500 cases of chloroform anesthesia in a children's hospital. H. Thorp (*Lancet*, Feb. 29, 1908).

The writer has noticed that delayed chloroform poisoning is more frequent between 3 and 8 years of age than either before or after that age. Subcutaneous injections of atropine were used before anesthesia to prevent the formation of mucus in the mouth and the subsequent absorption of the chloroform swallowed, but this had no influence in preventing the symptoms of delayed chloroform poisoning. It is possible that the anesthetic in part is excreted into the alimentary canal and reabsorbed from it. Therefore it matters little if the drug is swallowed or absorbed from the lungs. Corner (*Clinical Jour.*, May 29, 1912).

The writers found experimentally that fat administered to animals, and presumably stored in part in the liver, increased its susceptibility to the injurious action of chloroform. Opie and Alford (*Jour. Amer. Med. Assoc.*, Mar. 21, 1914).

Certain conditions are known to predispose the development of late chloroform poisoning. As to operations, torsion, incarceration, and strangulation of abdominal and pelvic organs, especially pyosalpinx, torsion of the pedicles of ovarian cysts, volvulus, incarcerated herniæ, and operative disorders about the anus, are most to be feared in this connection.

Suggestive coincidence in 12 cases of delayed chloroform poisoning attended by death on record; the operation had been done twice for torsion of the pedicle of an ovarian cyst and twice on account of large irreducible hernia of the omentum. In another case the thigh had been exposed to the Roentgen rays just before the operation. Sippel (*Archiv f. Gynäk.*, Bd. lxxxviii, Nu. 1, p. 167, 1909).

The late effects of chloroform narcosis are due to a diminished resistance, as from certain diseased conditions, such as septic or suppurative processes, cases of autointoxication, principally in connection with torsions, strangulations, and incarcerations of abdominal organs (twisting of pedicles of ovarian cysts, volvulus, obstructed herniæ, omental or mesenteric cysts). The danger of chloroform in these affections increases with the intensity and duration of the narcosis, and most likely with the size of the twisted organ or strangulated portion of intestine, and is less with a brief, uncomplicated incarcerated hernia. The danger, however, is always so great that chloroform narcosis is very strictly contraindicated in all the above conditions and in pyosalpinx. In such cases the quantity of chloroform which would be borne by some men and many other patients without difficulty would be sufficient to cause severe damage to the liver and kidneys, and subsequently the death of the patient. The causes of the decreased resistance to chloroform are to be found probably partly in autolytic changes or abnormal internal secretions which can aid the narcotic poison. Stierlin (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, Bd. xxiii, S. 408, 1911).

Prolonged anesthesia is the main cause, the majority of operations in which late poisoning has occurred having been long ones. This necessarily involves the use of a correspondingly large amount of chloroform—itsself a source of danger. The

latter is further increased when the patient happens to be a weakling or a diabetic or the subject of starvation, hemorrhage, or other conditions which have temporarily reduced the vital resistance of the tissues.

Certain individuals exhibit an idiosyncrasy or a susceptibility to this form of poisoning which it is difficult to explain. There are certain predisposing causes which favor this destructive effect of chloroform, among which are: (a) age—the younger, the more susceptible; (b) causes which lower the general vitality of the individual, and probably the vitality of the liver-cells, such as diabetes, previous recent anesthesia, infections from pus germs, diphtheria, intoxications from a dead fetus in the uterus, a gangrenous mass in the abdominal cavity, etc.; (c) exhaustion due to hemorrhage; (d) exhaustion due to starvation; (e) exhaustion due to wasting diseases, such as carcinoma; (f) lesions which have resulted in extensive fatty degenerations, such as occur in the limbs in infantile paralysis; (g) chronic diseases involving both liver and kidney, such as cirrhosis and nephritis. Bevan and Favill (*Surg., Gynec. and Obstet.*, Oct., 1905).

While the cases which present the symptom-complex described above usually terminate fatally, those of temporary icterus and the milder phenomena of the fatal form generally proceed to recovery. Such cases are not uncommonly met with, though at times their cause is unrecognized.

Report of 16 operations in which jaundice followed the use of chloroform out of 100 patients operated upon. Bilirubinuria was also present. In most cases jaundice developed on the second day after operation and lasted about three days. All but 1 recovered. Wechsberg (*Zeit. f. Heilkunde*, March, 1902).

Between the fatal cases of delayed chloroform poisoning of which not a few are recorded and cases with slight symptoms, perhaps unnoticed, there occur many of varying degrees of severity. There appear to the author to be four types of chloroform poisoning: (1) Ordinary so-called delayed chloroform poisoning, seen chiefly in children and young people. (2) A few cases of acute yellow atrophy of the liver after the administration of chloroform to pregnant women. (3) The hemorrhagic type, in which necrosis of the liver occurs, causing hemorrhages from the intestinal tract and kidneys, and even hemorrhage into the suprarenals. (4) A type in which the chief effect seems to be on the kidneys.

The author reports a case of chloroform toxemia in a child to whom fat was noxious; a death in an adult after chloroform administered during ptomaine poisoning; a case of chloroform toxemia characterized by jaundice and bilious vomiting; a fatal case of chloroform poisoning associated with asepsis and simulating meningitis; a case of laryngeal spasm, vomiting, and acetoneuria in an infant 2 days old, after delivery under chloroform; 2 cases of suppression of urine after the administration of chloroform, and a case of chloroform toxemia in a boy aged 5 years, with marked acetoneuria, notwithstanding the fact that glucose and bicarbonate of soda had been administered for two days before operation.

The following conclusions are offered: Never administer chloroform if etherization be possible, even to children or pregnant women. Avoid carbohydrate starvation, or any other form of starvation, before operation. If chloroform must be used, administer dextrose or sodium bicarbonate freely for days beforehand, especially if the patient be young or his condition septic. If postchloroform poisoning develops, administer freely soluble carbohydrates (dextrose) and sodium bicarbonate, in the worst cases injecting the dextrose

into the subcutaneous tissues and rectum, or even intravenously. W. J. McCardie (*Birmingham Med. Review*, Oct., 1912).

**Pathogenesis.**—The pathogenesis of late chloroform poisoning is still somewhat obscure. It is certain, however, that prolonged administration is the predominating cause, owing to the retarded elimination of the drug from the tissues this entails. Under these conditions chloroform has an elective action upon the liver, though affecting to a less marked degree the kidneys, heart, and muscles. The morbid changes are mainly those of fatty degeneration and necrosis, with autolysis of the necrotic cells, attended by an accumulation of polynuclear leucocytes. The hepatic lesions resemble closely those that attend phosphorus poisoning and other toxemias.

The writers have found an elective action on the liver, with the exclusion of all other organs with the exception of the kidneys. Introduced into the stomach of the dog, chloroform causes the following changes in the liver: Abundant hemorrhages, an enormous accumulation of polynuclear leucocytes in the interlobular spaces, degeneration of the hepatic cells, particularly a general marked fatty degeneration. Doyon and Billet (*Comptes-rendus*, May 8, 1905).

The delayed chloroform syndrome is due to a hepatic toxemia, the toxins producing it are hepatic toxins, and possibly the previous condition making its development easily possible should be described as liver insufficiency. Just as we have for a long time recognized a condition (uremia) in which we find arising from a variety of noxious agents, anesthetics, poisons, infections, pregnancy, etc., affecting the secreting cells of the kidney and preventing

their normal function a pathological condition accompanied with a certain definite symptom-complex; so we must now, we believe, recognize a condition involving the liver in which we find from a variety of noxious agents (anesthetics, poisons, infections, pregnancy, etc.) affecting the secreting cells of the liver and preventing their normal function a pathological condition which we must describe as hepatic toxemia accompanied with a certain symptom-complex, and showing certain changes *post mortem*. Bevan and Favill (Surg., Gynec. and Obstet., Oct., 1905).

The autopsies done on patients dying with all the symptoms of delayed chloroform poisoning almost invariably show the same macroscopic and microscopic changes, which are: pale and faun-colored liver, fatty degeneration or infiltration of the liver, the various changes of nephritis in the kidney, fatty degeneration of the heart, and fatty degeneration of the muscles of the lower limbs. The most important of these are those found in the liver—fatty degeneration and necrosis of the liver-cells; autolytic disintegration of the necrotic cells, and fatty degeneration of the cells which are not necrotic. The capillaries and blood-vessels do not seem to be involved, there is no thrombosis, and no inflammation or proliferative action. This condition is essentially an hepatic toxemia and the other changes are secondary in importance to those in the liver. Stevens (Jour. Mo. State Med. Assoc., Oct., 1909).

In dogs chloroform anesthesia lasting more than half an hour caused demonstrable fatty changes in the liver, first appearing in the intermediary zone. More prolonged and especially repeated anesthesia gives rise to necrosis, also beginning in the center and sometimes extending so that all the cells of the liver may become necrotic. There may be a more or less hemorrhagic extravasation. Calcium deposits surrounded

by giant cells were observed in necrotic areas and constitute a new observation. Fat necrosis also occurred in 1 case in the omentum and mesentery. Congestion and areas of hemorrhage in the gastrointestinal tract and serous membranes are frequent. There is great similarity between the experimental chloroform effects and those reported in fatal cases. Death is probably due to the presence of toxic substances of an unknown nature, which result from either abnormal metabolic processes or failure of the organism to neutralize toxic substances normally formed. Howland and Richards (Jour. Exper. Med., March, 1909).

A series of experiments and histological study of the lesions in animals and a fatal case showed that: 1. Chloroform is a poison, and when given to produce anesthesia will cause more or less damage to the liver. This is true for man and animals. 2. Chloroform anesthesia for a period of one or two hours invariably causes some central liver necrosis, and may cause a fatal result in dogs. 3. Animals vary widely in their susceptibility to this drug. Young animals as a rule are more susceptible than adults. 4. Chloroform anesthesia for thirty-five minutes may cause fatal poisoning in man with almost complete liver necrosis. 5. The pathology of chloroform poisoning is identical in dogs and in man. 6. The essential change is an extensive necrosis and fatty degeneration of the liver. There may be numerous ecchymoses and hemorrhages into the peritoneum or upper intestinal tract. The pancreas may show many fat necroses and ecchymoses. The kidney and heart may present a moderate grade of fatty degeneration. 7. Pregnancy is no protection against the poisonous action of chloroform anesthesia. Chloroform narcosis in pregnancy may cause extreme liver necrosis and placental necrosis with separation and hemorrhage. The fetus may show no liver necrosis. 8. Central necrosis

due to chloroform is uninfluenced by the blood-supply of the lobule. This necrosis is the same whether the hepatic artery is ligated or the portal blood excluded by means of an Eck fistula. 9. Ligation of the hepatic artery causes no change in the normal dog. 10. An Eck fistula produces a diffuse atrophy and little fatty degeneration, affecting principally the centers of the liver lobules. 11. Chloroform injected into the portal vein will cause scattered necroses, many of which are peripheral. 12. Chloroform injected into the hepatic artery will cause necroses of the same type, both peripheral and central, the latter predominating. 13. The liver necrosis becomes visible to the microscope only after six to ten hours. The explanation for this is not clear. 14. If an animal recovers from the chloroform poisoning, the repair takes place rapidly and brings the liver back to normal in two to three weeks. 15. Repair is effected by solution of the necrotic liver-cells and rapid multiplication of the remaining peripheral cells. 16. Repair goes on normally in a liver which is shut out from the arterial stream. 17. Cirrhosis does not follow extensive central necrosis and repair. Whipple and Sperry (Johns Hopkins Hosp. Bull., Sept., 1909).

Experimental study of the after-effects of chloroform on the liver, kidneys, and myocardium of rabbits. Of 25 animals anesthetized—inhalation by the drop method, lasting from one to two hours—8 died of after-effects of the drug (1 in three hours, 6 in twenty-two to forty-five hours, and 1 in one hundred hours); 8 others were killed at different periods to study the various pathological changes. In most of the animals which died as a result of anesthesia, microscopic examination of the liver gave nearly uniform results, viz., necrobiosis in the centers of the lobules, with marked deposition of fat-droplets, and similar but less pronounced changes as one proceeded to the peripheral zone of the

lobules, which was almost normal. Preparations from the kidney and myocardium showed marked differences, in contrast with the uniformity of the liver preparations. Changes were most constant in the *tubuli contorti* of the kidneys; the nuclei here were for the most part paler than normal, and the cells contained fat-droplets. In the heart, changes were even less conspicuous, degeneration being in general confined to increased clearness of the longitudinal striæ. In the rabbits killed at progressively increasing intervals, similar but less-advanced changes were noted. While fat appeared early in the endothelia, it was in those animals which were killed after a delay of twenty-four to forty-eight hours that degenerative changes were most prominent. These tests strongly suggested that the hepatic changes are the chief factor in the after-effects of chloroform. With regard to acid intoxication the author again emphasizes the importance of the rôle played by the liver, referring to the experiments of Van Embden and Kalberlah, who found this to be the only organ which formed acetone when blood was allowed to flow through it immediately after death. From a study of the process of re-elimination of chloroform after its distribution to various tissues, the writer is inclined to believe that the after-effects of this agent should be considered as the result of an acute affection of the liver consequent upon its absorbing chloroform-laden fatty substances from the blood. Muskens (Proceed. Royal Soc. of Med., March, 1912).

Judging from liver necrosis, pups seem to be immune to the poisonous action of chloroform anesthesia. This immunity or resistance is complete during the first week, very striking during the second and third, and usually disappears during the fourth week of life. Nests of blood-forming cells (blood-islands) are numerous in the sinuses of the liver during the first week and normally become pro-

gressively less numerous each week until the liver is almost free from these cells at the end of the fourth week of life. It is considered possible that these leucocytes in the blood-islands protect the liver against the specific action of a known poison, chloroform in this instance. Whipple (Jour. Exper. Med., March, 1912).

While two hours of surgical anesthesia will almost certainly produce considerable central liver necrosis and fatty degeneration in the dog, cat, rabbit, guinea-pig, rat, and mouse, one of the authors has shown that fetuses in utero and pups during the first three weeks of life have a marked resistance to late chloroform poisoning. This immunity might be explained by the "blood islands" or nests of blood-forming cells which are so conspicuous in the liver sinuses of fetuses and young pups. As these nests of nucleated red and white blood-cells become less and less numerous with advancing age, one can detect a lessening of this peculiar resistance to chloroform poisoning. One might, furthermore, expect to find interesting differences in the reaction to chloroform anesthesia on the part of animals with nucleated corpuscles. Further experiments were therefore performed by the authors which go to show that in the pigeon, frog, and terrapin there is a very marked resistance on the part of the liver to the poisonous action of chloroform. This may be due to the presence of great amounts of nuclear material in the blood-stream in contact with the liver-cell columns. Chloroform, in its action upon the liver-cells, attacks the *nucleus* particularly, and the injured cell shows early nuclear degeneration or necrosis. The protective action, therefore, centers in the liver-cell nucleus and presumably is affected by the presence of other nucleated cells in great numbers in intimate association with the liver strands. These nucleated cells (red or white) never show any signs of injury due to the presence of the chloroform. R. E.

Mosiman and G. H. Whipple (Johns Hopkins Hosp. Bull., Nov., 1912).

**Prevention and Treatment of Delayed Chloroform Poisoning.**—As emphasized by Bevan and Favill, the fact that the dangers increase with the amount of the drug employed and with the duration of the anesthesia constitutes a powerful argument for rapid operating and "in favor of limiting in every way possible the length of the anesthesia and the dose of the anesthetic." Time-consuming preparations should be made before and not during anesthesia. Carbohydrate food is thought to diminish the likelihood of delayed poisoning.

When the operation is completed, the patient should be encouraged to awaken as soon as possible, and by deep breathing—conducted with due prudence in view of the presence of an operative wound—to expel any residual chloroform in his lungs—brought there by the blood for expulsion—at the earliest possible moment, and thus facilitate its elimination from the tissues at large through the intermediary of its carrier, the blood.

Experiments cited which seem to prove that chloroform, however given, has far-reaching effects on the tissues and blood, and, consequently, upon metabolism and excretion. These effects are enormously increased when elimination is delayed.

Elimination may be delayed in many ways, and idiosyncrasy, or a number of undetermined factors, appears to influence the action of chloroform on animals.

A danger point occurs soon after the commencement of the administration by inhalation, and, although the establishment of equilibrium between absorption and elimination marks a point of less danger, the



safety is only relative. Immediately following the administration, changes of a degenerative nature may appear in many organs, and with delayed elimination the occurrence of delayed chloroform poisoning in some degree is certain to occur. Thus it seems proved that chloroform, however given, is an exceedingly treacherous drug, and that its use is fraught with grave danger.

The observation made by Noël Paton and Miss Lindsay, that the rate of elimination is improved by free ventilation and exercise in rabbits, suggests a method of minimizing risk of this sequel to chloroform anesthesia, and emphasizes the importance of not letting a patient "sleep it off." The condition seems to depend upon delayed elimination, and this may be due to the fixation of a certain proportion of the chloroform in the proteins of the serum or tissues. G. Herbert Clark (Glasgow Med. Jour., July, 1912).

#### **METHOD OF ADMINISTRATION.—***Position.*—The position of

the patient bears an important influence upon the results. When the splanchnic vasoconstrictors are paralyzed by injuries or poisons, such as chloroform, the influence of gravity becomes manifest, owing to dilatation of the abdominal veins, which entails a corresponding emptying of the heart and of the cerebral vessels; hence the numerous accidents reported witnessed in the dental position; that is to say, that employed by dentists for the removal of teeth. Death in sitting posture occurs from sudden cessation of the heart's action, through abdominal engorgement and cerebral anemia. That the brain may become ischemic is shown by 2 cases witnessed by Bedford Brown, in which, through extensive injuries of the cranium, large areas of brain proper were exposed. Chloroform

reduced the cerebral circulation. In 1 case in which the local hemorrhage was severe the latter subsided as soon as the patient was fully under the anesthetic.

For operations about the mouth or throat full extension of the head upon the trunk, while the patient is lying down, answers admirably, but, as shown by Buxton, it produces some congestion of the head and neck vessels, which in certain subjects induces a very undesirable amount of bleeding. If the extension is not exaggerated, however, and if the head is supported beyond the edge of the table so that the traction upon the anterior portion of the neck through an excessive extension is not too great, the abnormal bleeding can be avoided. For the removal of adenoid vegetations this position is of value. A small pillow or three or four towels adjusted to the edge of the table to support the head places the patient within easy reach of the surgeon and at the same time avoids the danger of excessive bleeding.

For operations in the vault of the pharynx, as in the case of adenoid growths, the blood is thereby prevented from flowing in the direction of the larynx: an element of danger, in many cases, when the position of the body is on a line with that of the region operated upon.

Oral operation sometimes makes it impossible to sustain anesthesia adequately through the mouth. This may be obviated by introducing a soft-rubber catheter through the nose, to the postnasal space, the free end of the catheter being connected with a graduated bottle containing chloroform into which a hand bulb can be made to pump air as needed. The

open method is much to be preferred, however.

The lateral position, recommended by many, is by no means always possible in stout persons, while short-necked subjects also bear this position badly. The anesthetizer should place a pillow well under the shoulders, giving just sufficient extension of the head upon the trunk for practical purposes.

A certain amount of care must be taken when the head is not fully extended, however, that the tongue, during the deep stage, be not allowed to fall back against the pharynx and thus tend to occlude the respiratory area.

Martin and Hare found that the passage of air through the glottis was facilitated and the epiglottis and soft palate kept raised by supporting the head as it would be were a block of wood about four inches high placed under the occiput. A roll of towels can be used for the purpose.

*Influence of Atmospheric Conditions.*—When the air is surcharged with moisture the chloroform condensation in the pulmonary air-cells and its subsequent entrance into the blood are impeded; the stages of narcotism will, by this, be prolonged. Recovery is also slower. Syncopal attacks in a moist atmosphere are more likely to terminate fatally. Again, the moisture which should escape from the air-passages cannot do so when the atmosphere is too saturated and the tendency to waterlogging of the lungs under chloroform is increased. Benedicenti found experimentally that the action of chloroform is more rapid but less lasting if the atmospheric pressure is reduced. The elimination of chloro-

form by the lungs is much more rapidly effected in animals subjected to very low pressure.

The temperature also bears a marked influence. When it is high, the volatilization is more rapid, the diffusion and condensation are increased, and both the onset and the recovery are more rapid by favoring the exhalation of chloroform. The safest temperature is 60° to 70° F.; a higher rather than a low range is best. As observed by Neve, in India the mortality from chloroform does not exceed 1 in 8000 cases, and in some of the largest institutions it is less than 1 in 20,000 cases. Safety is not related to any special constitutional condition of Hindu races and but little to their habits. It is due to the warm atmosphere, which favors the rapid action of the drug and its rapid elimination. To obtain similar safety in climates such as that of England, it would be advisable to operate in well-ventilated rooms, with a temperature not below 70° F. Anesthesia should be produced gradually, with the chloroform diluted with plenty of air.

*The proportion of chloroform to the air inhaled* for anesthetic purposes should not exceed 2 per cent. This should be reduced, as advised by the British Special Chloroform Committee in 1910, gradually as the subject is weaker, until in marked weakness or in the presence of a grave disease the proportion is reduced to 0.5 per cent.

The proportion of air and chloroform administered is roughly graded by the rapidity with which the latter is poured on the inhaler and the proximity of the latter to the face. Instruments have been devised for

the purpose, but they do not seem to have given satisfaction.

*Preparation of the Patient.*—The patient should be in an entirely loose garment and in the recumbent position. A quiet, well-ventilated, and well-lighted room should be selected.

Any foreign body, such as false teeth, tobacco, or any accumulation of mucus, should be removed from the mouth, nasopharynx, and nasal passages.

All solid food should have been withheld for at least four hours and no liquid food given for at least two hours before the administration of the anesthetic. This recommendation is of the greatest importance, for the regurgitation of food when the patient is under the anesthetic may, by entering the larynx, cause asphyxia.

The patient's fear should, as much as possible, be allayed by kindly and encouraging words, death being sometimes caused by heart syncope, resulting from fright. A show of surgical instruments should be avoided. Mental factors are influential causes in the production of chloroform death. Fear and anxiety can cause profound circulatory disturbance, and this condition may predispose to danger when an anesthetic is given and even cause death by cardiac inhibition in the first stage.

If the operation is at all to be prolonged or be of such a nature as to cause severe pain in the waking state, an hypodermic injection of **morphine**,  $\frac{1}{6}$  grain, should be administered twenty minutes before the chloroform is given. It does not tend to depress the respiration or cardiac action, as some contend. This occurs only when the dose is excessive. It also tends to inhibit morbid reflex action.

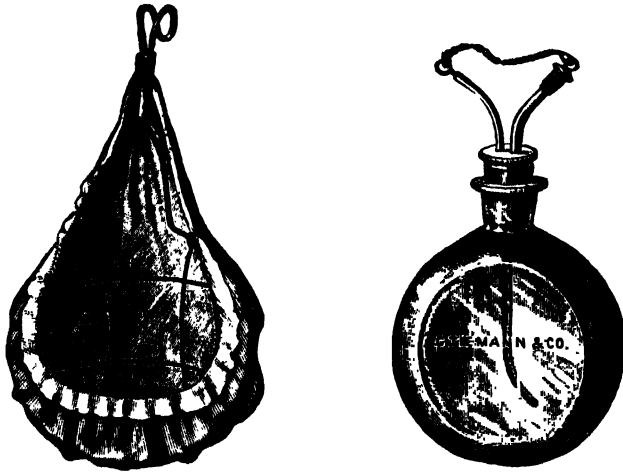
To avoid morbid reflex influence from the nasopharyngeal mucous membrane through the fifth nerve, before chloroformization, the writer advised an injection of 1 c.c. (15 minims) of the following solution: **Morphine**, 10 cg. ( $1\frac{1}{2}$  gr.); **atropine**, 0.01 cg. ( $\frac{1}{6}$  gr.); **sparteine**, 1 Gm. (15 gr.); distilled water, 10 c.c. ( $2\frac{1}{2}$  dr.). Or, the nasal mucous membrane and pharyngoglottic region may be painted with a concentrated solution of **cocaine**. Laborde (Semaine médicale, May 14, 1902).

Study of the behavior of the reflexes under chloroform has convinced the writer that some of the functional heart and respiration disturbances are the result of reflex action from the field of operation. Certain regions are more liable than others to elicit such reflexes. Among them are the testicles, the spermatic cord, hernia, the peritoneum, and all points where the mucous membrane joins the skin, as at the anus. The intensity of the reflex also varies with the nervous condition. In anemia, infections, intoxications, psychoneuroses, etc., the reflex excitability should be tested before an operation, and chloroform should be used with exceptional care in the cases with hyperexcitability. Chloroform is unable to abolish all reflex action, especially in the more distant regions. The danger from chloroform syncope is imminent throughout, but it is most marked toward the close of the anesthesia from the depression induced by the chloroform. The writer favors the administration of **morphine** an hour or more before the operation on all extremely excitable patients, and for all operations in regions known to be particularly liable to induce reflex action. Deep chloroform anesthesia should be reserved for the stage of the operation in which it is indispensable, and for those operations which require relaxation of the muscles. Since he has preceded the chloroform with morphine he has never had any mishaps from chloroform or ether. Very

much smaller amounts are required when a sedative is given beforehand. Messeri (Jour. Amer. Med. Assoc., from Policlinico, Nov., Surg. Sect., 1908).

*Administration and Dose.*—Many instruments have been devised for the purpose of administering anesthetics in general, but these are seldom employed outside of hospitals. Except under certain conditions, when the anesthetic is administered in the presence of gaslight, the simplest way to

face; it should be kept from three to six inches above it, according to the air dilution the anesthetizer desires—a factor, we have seen, which depends upon the condition of the patient. Besides, this avoids all sensation of smothering or choking which causes the patient to struggle. In the case of a fair-skinned female patient, it is advisable to apply vaselin or cold cream where the chloroform vapor is likely to touch the skin.



Esmarch's chloroform inhaler.

apply chloroform is on a towel or handkerchief, or a cone or funnel may be made with a folded towel into which the anesthetic may conveniently be dropped. Better still, a simple layer of open-meshed flannel may be applied over a cone-shaped wire frame. Esmarch's inhaler shown herewith serves admirably the same purpose. This has the advantage of giving free passage to the air, which then mixes freely with the anesthetic.

Both on account of its irritant action and of the imperative duty of allowing plenty of air (at least 98 per cent.) to be inhaled with the anesthetic, the cone should not touch the

A drop-bottle should be employed for the anesthetic, the pouring-out method formerly employed being a dangerous procedure. That shown alongside Esmarch's inhaler renders it possible to limit to a single drop at a time the quantity administered.

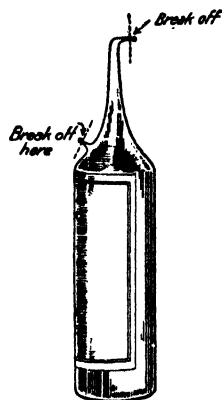
A convenient device for the same purpose is available on the market, the "dropper ampoule." It presents the advantages of containing pure chloroform, an important feature in the prevention of complications, and of being hermetically sealed before it is used. It contains only enough chloroform for one case, thus removing any danger from the chloroform

left unused. The cuts are self-explanatory. The first figure shows the ampoule before it is ready for use, and the second while it is being used.

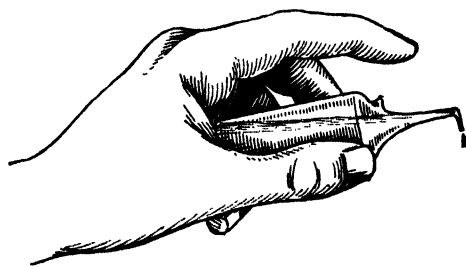
The dropper ampoule is simpler than any other dropper in its construction, its preparation, and use. It is the most economical dropper, because its capillary ending insures the smallest possible drop, which results in a minimal consumption of chloroform. It is the most convenient and compact package of chloroform, since it obviates the necessity of carrying an extra dropper, and is so packed that it can be carried with perfect security in the emergency or obstetrical satchel. It is the safest dropper, because it uses the least amount of anesthetic consistent with adequate narcosis and the anesthetist has perfect control of the drip, being able to regulate the frequency of the drop at his discretion. Personal experience has proved conclusively that patients accept narcosis much more readily with the use of the dropper ampoule than with any other dropper, because the minimal amount of chloroform used allows for a correspondingly greater admixture of air. The stage of excitement is lessened or entirely obviated, narcosis supervenes more rapidly, and cyanosis is of very infrequent occurrence. Also during long anesthetics there is no tendency on the part of the patient to collapse from shock due to saturation with the anesthetic. Postoperative nausea and vomiting are conspicuous by their absence. Also no cases of delayed poisoning have so far been recorded in any of the personal experiments. McMechan (N. Y. Med. Jour., July 17, 1909).

The important feature, as already emphasized, is to supply enough air to enable the patient to breathe regularly, as usual. Chloroform should *never be pushed*. This old-time defect has caused many deaths during

and after anesthesia, through cardiac arrest in both the first and second stages, and by cumulation of chloroform in the tissues, especially the liver, which is the main factor in the dangerous "delayed" poisoning (*q.v.*). The exhalation of the anesthetic from the lungs should always be free. Any gasping or choking should cause the



The dropper ampoule before using.



The dropper ampoule in use.

anesthetizer to raise the inhaler so as to increase the supply of fresh air for a short period, until all signs of discomfort have disappeared. Coughing indicates that the air inhaled is too heavily charged with chloroform, while struggling in the first stage shows that the patient is feeling the want of air—a terror-inspiring sensation which in itself is a source of danger.

When the patient is brought into the anesthetic room absolute quiet is

insisted upon, for it should be remembered that all sounds are very much magnified to a patient who is about to pass into the second stage of anesthesia. The friends are kindly but firmly excluded, and the writer prefers even not to have the family physician present, as he is very apt, in his anxiety, to tell the patient with many reiterations that he is all right, and that he (the physician) is right there and will stay by him; or, he instructs the patient to take deep breaths, etc. The subject for anesthesia should never be told to breathe deeply, nor be requested to count; both have a tendency to arouse the patient's fears and disturb tranquillity.

When the anesthetist is ready to begin, the patient is told in a low voice to close the eyes and go quietly to sleep; and occasionally, during the first two or three minutes, it should again be suggested in the same low tone that he try to go to sleep, and to keep the eyes closed; or, "Don't mind the smell in the beginning," etc. Never say, "Don't mind the smothering sensation"—that is sure to cause anxiety. W. P. Burdick (*Therap. Gaz.*, June 15, 1912).

The patient is ready for the operation when the cornea becomes insensitive. Stertorous breathing usually begins at about the same time and the muscles become relaxed, the arm when raised falling inertly. As soon as either of these signs appears, the anesthetic should be withheld, and the operation begun, the anesthetic being thereafter administered now and then a drop or two at a time—twenty to thirty per minute—only just enough to keep the patient in surgical anesthesia until the operation is completed. At all times the patient should be supplied with an ample proportion of fresh air, 0.5 per cent. of chloroform being sufficient in most cases to keep the patient anesthetized.

The amounts of chloroform absorbed late in anesthesia are not great. When once anesthesia has been fully established, the dosage of the chloroform should be adjusted to prevent the blood giving up its chloroform, rather than with the idea of pouring more of the drug into the organism. The dosage of chloroform required to abolish the corneal reflex constantly decreases with the prolongation of anesthesia, sinking at the end of five hours to as low as 0.5 per cent. When the organism is fully saturated with chloroform a very low percentage is sufficient to maintain anesthesia. B. J. Collingwood (*Jour. of Physiol.*, May 9, 1905).

The exceptions are where traction upon the abdominal organs, breaking of adhesions, forced extension for ankylosis, forcible dilatation, etc., or any procedure capable of causing considerable pain is inevitable. Then the 2 per cent. is resumed as needed, but only to maintain the patient under surgical anesthesia and *not* under deep anesthesia. According to Snow, chloroformization should be complete for the operation, in two minutes for infants, three for children, and four or five for adults. In less highly trained hands, however, it requires from eight to ten minutes.

As to the quantity required to produce narcosis Kionka found, in a series of special researches, that the dose required was relatively small. Narcosis was obtained when the air contained from 0.15 to 1.3 per cent. of chloroform, or 2.1 to 7.9 per cent. of ether. The minimum quantity of ether necessary to produce anesthesia could be greatly exceeded without endangering life, and narcosis could be prolonged by using the same dose, while, under similar conditions, chloroform invariably caused death of the

animal. Sleep under ether, when once established, could be maintained with a smaller dose than that required to produce it. From the beginning chloroform caused early arrest of heart and respiration.

One of the great errors usually made is that the same routine quantity is administered to all patients. As long ago emphasized by Buxton, every individual requires a specific dose, the drunkard and athlete requiring more than the pale, frail, anemic subject, who requires very little.

When the operation is terminated, the patient should be encouraged to awaken, and to rid his lungs of chloroform, as soon as possible, by deep breathing—due care, of course, being taken to interfere in no way with the operated area. The patient should be removed to another room, where fresh air, free of chloroform, is available; or, the room in which the operation was performed should be freely ventilated. Prolonged contact of chloroform with the tissues through its carrier, the blood, may cause late and often fatal poisoning.

Chloroform can be administered during sleep where there is undue fear, or, as in children, the opposition might prove too strenuous or hurtful to the patient.

The writer has given chloroform to two children without awakening them. The anesthetic was given on a modified Skinner mask, which was held slightly away from the face. Before the corneal reflex disappeared, the child allowed the mask to be laid on the face, and, although some slight movement of the head was made, there was no disturbance. The pupil, of course, could not be examined from the beginning of the anesthetic, but when first examined was moderately contracted, and re-

sponsive to light. Jefferiss (Brit. Med. Jour., June 24, 1911).

The stages of chloroform narcotism as given by Snow and Buxton are divided into four:—

The *first* stage, from the commencement of inhalation to the loss of conscious control of the limbs.

The *second*, to the stage of loss of conjunctival reflex and rigidity of the muscles.

The *third*, or surgical, stage, when the muscles are relaxed (in the main), the corneal reflex is lost, and the pupil is contracted.

The *fourth* stage, when the medullary centers are affected, the pupils dilate, the respiration gradually fails, the muscles are absolutely relaxed, the sphincters cease to act, and the circulation is weakened.

Beyond this stage convulsions occur, the breathing ceases, and the heart and circulation come to a standstill. The complete relaxation of the muscles can, in some cases, be arrived at only by the patient's entering the fourth stage, and, in the case of chloroform, such pushing of the anesthetic can only be accomplished by seriously jeopardizing the patient's life. Bell has noted that the symptoms of approaching danger under chloroform always appear in the following order: (a) *coughing*, (b) *gasping*, (c) *choking*, and (d) *struggling*. If, at the first appearance of coughing, the vapor is given more diluted, no further difficulty will arise.

**Intratracheal Insufflation.**—According to B. M. Kicketts (Med. Rec., Sept. 19, 1914), extensive laboratory experiments, verified by post-operative results, prove conclusively that so far as respiratory complications are concerned, *intratracheal insufflation* is an innocuous procedure, even in the presence of lobar pneumonia. Also, the

recurrent air stream through the trachea precludes the possibility of aspirating vomited material or hemorrhage from the pharynx. A silk woven catheter 30 cm. long, and of a diameter one-half that of the glottis, serves as the best intubation tube. Its introduction is best accomplished after the induction of narcosis by ethyl chloride-ether or nitrous oxide-oxygen-ether.

Guisez (Bull. Acad. de méd. Par., lxxvi, 245, 1916) introduced a new method of anesthesia for operations upon the head and neck—*direct intubation*—in which it is possible, by means of a special tube introduced through the mouth and with the aid of direct laryngoscopy, to administer directly into the trachea a very exactly proportioned mixture of air and chloroform. It differs from the American method of insufflation in that both inspiration and expiration are done directly through the intralaryngeal tube. Preliminary narcosis is induced by the mask in the ordinary way. The duration of the operations on the mouth and pharynx is greatly shortened. It obviates mechanical obstruction.

**UNTOWARD EFFECTS AND ACUTE POISONING.**—*Predisposing Causes.*—The chances that morbid phenomena will occur during anesthesia have been estimated at 1 in 1500, provided average care has been taken in determining whether the case be not one offering unusual chances against a successful administration. But in *all* cases certain allowances must be made not only for previously undiscovered morbid conditions which may suddenly bear their influence upon the issue, but also for known conditions which also modify the form of issue.

The impression prevails that children are less vulnerable to the toxic action of chloroform than adults, but, as Owen urges, there is always risk in giving chloroform or any other anesthetic to a child. This risk, however, is diminished in proportion as

the vapor is administered in a careful manner and by a well-instructed person. It is important also to bear in mind, in this connection, that the general impression that children very rarely succumb to the influence of chloroform is erroneous. The many deaths in children ranging from early infancy to 15 years of age have served to emphasize this fact.

On the other hand, the fear that untoward results will follow the use of an anesthetic in patients of advanced age is equally exaggerated, as shown by a large series of cases reported in which no unusual effect was witnessed. Heath, for instance, administered chloroform to a woman 94 years old, to reduce a dislocation. The patient bore the anesthetic calmly and easily. Indeed, acute suffering is a prolific source of fatal shock in old people, and anesthesia thus becomes a life-saving agent in them.

As regards the increased liability to untoward effects through disease, Reynier found that fatal accidents are liable to occur, according to the more or less great resisting power of the various cells affected during the anesthetization. Thus, in alcoholics, whose cerebral cells are in an abnormal state, delirium is observed, which may reach the stage of delirium tremens; but in these subjects, also, myocardial degeneration is probable, and cardiac failure is likely in proportion. In hysterical subjects all varieties of hysterical attacks may occur, even paralysis and syncope. The same is the case in epileptics. In morphinomaniacs only slightly intoxicated, chloroformization is easily and rapidly accomplished; in others, on the contrary, it is more dangerous.



In ataxic subjects the period of medullary excitement nearly always gives rise to reflexes which may arrest the respiration and heart movements.

To these morbid conditions must be added those enumerated and involving the circulatory, respiratory, and urinary systems, and prolonged abdominal operations, strangulated hernia in old and exhausted subjects, colotomy and colectomy, etc., to which reference has already been made. Extra watchfulness should be observed in *all* such cases, and shock anticipated by measures calculated to preserve the tone of the cardiovascular system.

*Pain* has caused death under chloroform within a very short time after the commencement of inhalation, or when comparatively trifling, although painful, operations were to be performed (extraction of teeth, etc.). *Shock* during *imperfect anesthesia* accounts for these cases, which are observed when a painful operation is started too soon after the administration of chloroform has begun. Its mechanism may be similar to that of reflex cardiac arrest due to irritation of nasal branches of the fifth pair in the nasal cavities, which may cause instant death during the first stage of anesthesia, but it is probably often associated with exhaustion of the vasomotor center, due to the excessive afflux of sensory impulses from the periphery.

Closely connected with the production of shock is *fear*, which tends greatly to increase the chances of cardiac syncope, through the exaggerated functional tension induced. Even a small amount of chloroform is capable of inducing a fatal issue under these circumstances. There is

a marked difference in this particular between Europeans and Hindoos,—a fact which has served to markedly decrease the mortality of anesthesia in India.

Too little importance is usually attached to *struggling*, which, according to Lawrie, is produced (1) by fright, leading to purposeful resistance; (2) by choking or asphyxia from overconcentration of the vapor, owing, generally, to the cap being held too close to the face at first or afterward when the chloroform is being renewed, and (3) by intoxication,—i.e., the so-called “struggling stage.” Dudley Buxton considers the struggling of intoxication as extremely dangerous. The breathing is then irregular and the amount of chloroform in the circulation is considerable, anesthesia being nearly complete,—factors markedly increasing the chances of cardiac syncope and general anoxemia.

The inhaler should be removed from the face for a few respirations, which does not necessarily cause a break in the narcosis, as chloroform still remains in the air-cells, and, as soon as respiration has resumed its normal character, the chloroform is reapplied.

Certain regions are especially prone to encourage cardiac syncope when submitted to *rough handling* in surgical procedures. Traction upon the omentum and undue manipulation of the intestines and other viscera are probably the most active factors of this kind. Operations upon the anus have also shown a tendency in this direction. Operations that would be attended by great pain without an anesthetic seem to show the greatest tendency to produce circulatory failure.

Excessively prolonged *fasting* prior to chloroform is also dangerous, owing to the lowering of tissue oxidation and the slowing of metabolism entailed. Moreover, it tends to promote acidosis. All these factors, in turn, by causing debility impair the patient's ability to stand anesthesia with safety. Christopher Heath, when an operation was likely to be prolonged, administered an enema of beef-tea half an hour before the administration of the anesthetic. Others give a little alcohol, or a heart tonic, especially *digitalis*, if the heart's action was weak. *Epinephrin* has recently been used in this connection.

If a few grains of *quinine* be administered within twenty-four hours before an operation, it will be found that the heart's action is improved, and maintained right through the time of the operation, regardless even, perhaps, of the amount of the anesthetic used. The writer gives the drug in the form of the hydrochloride, with some diluted hydrochloric acid. Edward Jepson (*Brit. Med. Jour.*, Dec. 3, 1904).

Experiments were performed by the authors upon guinea-pigs which showed that prolonged chloroform anesthesia causes changes involving both the cortical and medullary portions of the adrenals. In the former the distribution of the fat is altered, probably also its amount and possibly its nature. After the anesthesia the fat is seen to have spread inward from its normal situation, reaching nearly to the inner reticular zone of the cortex. In the medulla the chromaffine property and the epinephrin are found to have diminished or even entirely disappeared.

In view of the importance of the adrenal glands, the writers consider it clearly shown by the above facts that alterations in these glands play a part in certain of the fatalities following chloroform anesthesia, as

well as in operative shock, the manifestations of which—asthenia and feeble pulse—are symptoms of adrenal insufficiency. Sudden, unexpected deaths occurring in the evening, on the morrow, or on the third day after an operation are frequently attributed to embolism. But a patient succumbing to embolism will cry out, complain of intense pain, or present asphyxial phenomena, sometimes convulsions, whereas in many post-operative deaths no such happenings are witnessed, the patient being frequently simply found dead in the morning and showing tuberculous involvement of the adrenals at autopsy.

For these reasons one of the authors has for the last three years been giving subcutaneous injections of epinephrin regularly to all cases operated. The dose used is 0.0004 Gm. for ordinary operations and 0.0006 Gm. for those involving considerable traumatism. At first the injection was given at the end of the operation; later, at the start of the anesthesia. After experience with over 1000 cases this author thinks it justifiable to affirm that the giving of epinephrin in this way is of great advantage to operative cases. It regulates the narcosis, and it lessens or even in most instances eliminates operative shock. He is also convinced that it is capable of preventing certain sudden postoperative deaths which appear to be due to adrenal insufficiency. Where a patient remains asthenic for twenty-four hours after the operation, further injections of 0.0004 Gm. of epinephrin may be given. Delbet, Herrenschmidt, and Beauvy (*Revue de chir.*, April, 1912).

The writers found experimentally that the inhalation of *amyl nitrite* definitely increased the dose of the chloroform solution required to cause death in animals. Gilman, Devine and Barber (*So. Med. Jour.*, Oct., 1915).

**Symptoms of Collapse.**—As a rule, the *preliminary signs* of collapse are sufficiently well marked, and if ob-

served in time many a catastrophe may be averted. These signs are circulatory and respiratory.

The circulatory sign is the presence of increasing pallor, not amounting to absolute blanching.

*Failure of respiration* is marked by a peculiar type of breathing, in which *expiration is extremely short and inefficient, while inspiration is sudden, forcible, and gasping*, often accompanied by falling of the lower jaw, and spasmodic clonic contraction of the chin depressors and muscles of the neck. The inspiratory gasps are irregular and broken, and occur with increasing slowness until the condition of sudden collapse ensues.

This type of breathing is precisely similar to that which is often seen in a patient dying of respiratory failure from other causes.

Syncope of the heart is rarely primary in anesthesia, though this may be at variance with the common belief. This has been the writer's clinical and laboratory experience. In every animal, about 20, respiratory paralysis preceded cardiac failure by a minute or more. Thos. F. Lowe (personal communication), in over 2700 anesthetics, states that in the only death during this series chloroform was being administered, but the heart was functioning at least half a minute after breathing had ceased. Mary Magaw, referring to chloroform, in an article entitled "Review of Over 14,000 Surgical Anesthetics," quotes Finney as follows: "It is well to watch the character and rate of the pulse, but of far more importance to watch the respiration as the earliest indication of danger." The Hyderabad Commission maintained in a most carefully prepared report that primary heart-failure did not occur. C. S. White (Surg., Gynec. and Obstet., Oct., 1909).

Under light chloroform anesthesia the ventricular irregularities may terminate in ventricular fibrillation and death of the heart: (a) As a reflex from sensory excitation. (b) As a result of an intermittent administration of the anesthetic. (c) From the nervous excitement accompanied by struggling induced in the earlier stages. G. Levy (Heart, vol. iv, No. 4, 1913).

Under the influence of chloroform the *pupil* first dilates and then contracts. The dilatation of the pupil of incomplete chloroform narcosis is due to sympathetic impulses which give rise to reflex inhibition of the center of the third nerve. In complete narcosis the contracted pupil is due to the complete subjection of the cerebrum, while the unopposed third-nerve center remains active, all cerebral reflexes being now barred. In dangerous narcosis, the third-nerve center itself becoming poisoned, its action no longer controls the pupil, which *dilates and grows less and less sensitive to light, while the globe becomes fixed*.

Fixation of the eyeball, together with the stertor of breathing and the sluggish pupils, forms the contrast between the danger stage of chloroform sleep and the second stage, when dilatation of the pupil is associated with shallow breathing, efforts at vomiting, pupils reacting to light, and return of conjunctival and other reflexes. The period of going under is now generally considered as the one of most danger.

Case of poisoning in which there appeared blebs filled with serum on the lower extremities; these were largest on the plantar surfaces of the feet. C. E. Hyde (N. Y. Med. Jour., cvii, 67, 1918).

The first morbid action of *actual collapse* may occur at the outset, be-

fore the patient is anesthetized. Suddenly the patient becomes *deadly pale*, the *heart stops*, and *syncope* follows.

The part played by reflex action in the production of syncope is now fully recognized. Laborde noted, in 1890, that the heart of the monkey was immediately arrested by the irritative action of chloroform vapor on the nasal distribution of the fifth part, and observed that the application of a solution of cocaine to the nasal mucous surfaces prevented the untoward result. Rosenberg, Guttman, and others have utilized this prophylactic measure during surgical anesthesia, and have lauded its merits.

In order to prevent as far as possible this cause of death, which is always imminent, as soon as one approaches the nose of a patient with a compress soaked with chloroform it is necessary to decrease the unnecessary excitement of the patient and the susceptibility of the terminal expansion of the fifth cranial nerves. The best means of accomplishing this purpose consists in giving a preventive injection of an appropriate dose of a mixture consisting of hydrochloride of **morphine**, 0.1 Gm. ( $1\frac{1}{2}$  grains); sulphate of **atropine**, 0.01 Gm. ( $\frac{1}{4}$  grain); sulphate of **spar-teine**, 1 Gm. (15 grains); distilled water, 10 Gm. ( $2\frac{1}{2}$  drams), to every individual to be chloroformed. Irrigation of the nasal mucous membrane and of the pharynx and glottis with a solution of **cocaine** is also of great benefit in suppressing the susceptibility of these regions. It is also necessary to see that the tongue remains well forward in the mouth during the entire duration of the chloroformization, thus avoiding sliding of this organ backward over the orifice of the glottis, thereby provoking asphyxia. Laborde (Medical News, July 5, 1902).

Whether in the first stage or later, when surgical anesthesia is obtained,

the symptoms are the same, according to Guthrie: Sudden and complete blanching of the face takes place, leaving it of a ghastly gray hue. The term "pallor" conveys no idea of the actual appearance. The eyelids fall open; the eyeballs are fixed in the upward position, with pupils fully dilated, as under extreme atropinism. At the same time the cornea becomes glazed and sticky, giving an appearance which, once seen, is never forgotten. It can only be described in a somewhat fanciful manner by saying that the light seems to fade from the eye as does the color from the cheek and lips. It is the undoubted look of death.

The appearance of a person in a dead faint, or just after a severe accident, depicts but feebly that which obtains in chloroform collapse.

*The pulse and cardiac impulse are at these times no longer to be felt. Respiration commonly ceases at the moment when the blanching and stoppage of the pulse occur*, but at times a few feeble and irregular inspiratory gasps are subsequently drawn. The patient is to all appearances dead.

In some cases lividity, accompanied by turgescence of the veins of neck and face, immediately precedes the blanching and look of death, and is coincident with the stoppage of respiration. This may be replaced by cyanosis. In children, cyanosis, except where actual mechanical asphyxia has been produced, is less apparent than pallor.

**Methods of Resuscitation.**—When there are indications of syncope, no time should be lost in ascertaining the degree of danger present and the most active measures, short of heart massage, should be resorted to from

the start. The most effective of these are:—

1. **Inversion of the patient, with artificial respiration.** Howard A. Kelly recommends the following plan, which combines inversion and artificial respiration in an especially effective manner: "On the first indication

the edge of the table, where it hangs extended and slightly inclined forward. The patient's clothing is pulled down under the armpits, completely baring the abdomen and chest. The operator, standing at the head, institutes respiratory movements as follows: Inspiration, by placing the



Kelly's method of resuscitation. (Operative Gynecology.)

of failing respiration the administration of the anesthetic should be instantly suspended and the wound protected by a fold of gauze. An assistant steps upon the table and takes one of the patient's knees under each arm and thus raises the body from the table until it rests upon the shoulders. The anesthetizer in the mean while has brought the head to

open hands on each side of the chest posteriorly over the lower ribs, and drawing the chest well forward and outward, holding it thus for about two seconds; expiration, reversing the movements by replacing the hands on the front of the chest over the lower ribs and pushing backward and inward, at the same time compressing the chest. The success of

the maneuver should be demonstrated by the audible rush of the air in and out of the chest."

The following plan of resuscitation was pursued by **Maas**, and, after over an hour, in each case successfully: The mouth was opened, the tongue drawn forward, and the epiglottis

Sylvester's method of artificial respiration was adopted, and more vigorous pressure made over the breast. A similar course was adopted in the second case. The maneuver is thus performed: The operator stands upon the left side of the patient, and presses, with quick, strong move-



Kelly's method of resuscitation. (Operative Gynecology.)

raised. The precordial region was then compressed thirty or forty times a minute (the frequency of respiration). Whenever this was stopped, syncopal symptoms again appeared. Subsequently tracheotomy was performed, as it was difficult to keep the air passages free; but this did not assist the circulation. The respirations becoming almost imperceptible,

ments, deep down in the region of the heart with the fingers of the right hand, while the ball of the thumb is placed above the left clavicle. The number of compressions is 120 or more per minute. The left hand should seize the patient upon the right side of the thorax.

Leedham Green tried the König-Maas method in a child apparently

dead, using rapid compression (about 120 per minute) of the precordium, and obtained recovery. Seven minutes had elapsed during which neither heart-beat nor respiratory effort could be detected.

2. Simultaneously with inversion and artificial respiration: Injection of 4 minims of a 0.5 per cent. solution of **atropine** directly into the heart muscle with a hypodermic needle. According to Rendel Short, the value of this procedure has been abundantly proved for vagus inhibition, experimentally and clinically.

Or, the intravenous injection of **saline solution**, 1 pint (500 Gm.), injecting drop by drop into the tube carrying the solution to the median cephalic vein 15 minims (1 Gm.) of **pituitary extract** or **adrenalin chloride** (1:1000).

In postoperative shock **pituitary** has all the advantages of adrenalin, namely, the power to increase the vascular tone and raise the blood-pressure without temporary reaction of the latter. In 3 cases of shock after operation it gave excellent results. The writer uses a 20 per cent. solution, and for adults gives an intramuscular injection of 1 c.c. (16 minims). In each case, almost immediately after the injection, the pulse became strong and regular, and remained so. This vasoconstrictor substance is derived from the posterior or infundibular portion of the gland. Wray (Brit. Med. Jour., Dec. 18, 1909).

Experimental study of the therapeutic value of **pituitary** or infundibular extract in shock, uterine atony, and intestinal paresis, conducted by injecting an extract of it into animals and by observing the effect of the removal of it in part or wholly. It raises the blood-pressure, and even better when the animal is in a condition of shock than in a normal

state. Moreover, it keeps the pressure raised for several hours, whereas the effect of adrenalin in this respect is but temporary. It will not take the place of salines, for on the latter rests the responsibility of maintaining the improvement produced by any remedy. W. H. Bell (Brit. Med. Jour., Dec. 4, 1909).

Or, the intramuscular injection (biceps preferably) of 10 minims (0.65 Gm.) of **adrenalin chloride** (1:1000) in a hypodermic syringeful of saline solution. (Illustrative abstracts of the value of adrenal and pituitary extracts have already been given. See article on Animal Extracts in the first volume.)

Strychnine has been found valueless under these conditions; the same may be said of amyl nitrite, hydrocyanic acid, and other depressants.

3. If the measures detailed above fail **cardiac massage** is necessary, the abdomen being at once opened by the surgeon. The right hand is introduced under the diaphragm with the palm facing anteriorly; two fingers are then placed posteriorly to the heart (the diaphragm intervening) and in such a way as to compress the ventricles against the chest-wall. This is done rhythmically about sixty times a minute.

Massage of the heart as a means of resuscitation tried in dogs. The procedure of massage of the heart shown to be both sound therapeutics and perfectly justifiable in all cases of death from chloroform or any other anesthetic, as well as from drowning and allied conditions, when all other means of resuscitation have failed. R. C. Kemp and A. W. Gardner (Boston Med. and Surg. Jour., May 21, 1903).

Case of a woman aged 32 years who was operated upon under chloroform anesthesia for adherent ovarian

cyst. Fifteen minutes after the commencement of the operation the patient, without any previous respiratory, circulatory, or pupillary symptoms, suddenly became cyanotic and pulseless, cessation of respiration in this case following and not preceding that of the heart. Artificial respiration was then resorted to and continued, and the usual remedies administered. After two minutes had elapsed and no reaction had been established, the operator introduced his left hand into the abdominal cavity, pushed it along the anterior abdominal wall until the diaphragm was reached, then turning the hand, palm upward, easily grasped the heart through the relaxed and intervening diaphragm. There was an entire absence of heart action. After placing the right hand over the precordial region externally, bimanual rhythmical compression of the heart was performed at the rate of about sixty times a minute. After thirty seconds a slight beat was felt by the left hand. The heart then began slowly to beat, gradually increasing both in strength and rapidity of beat, until after the end of one minute the beats registered about 80 to the minute, and respiration was partially re-established. About two minutes later respiration was normal; pulse, 80. Cohen (*Jour. Amer. Med. Assoc.*, Nov. 7, 1903).

Five minutes seems to be the usual limit for possible revival of the arrested heart action by massage. In only a very few instances was the patient resuscitated after a longer interval than this. The list of successes includes 6 cases published during the last two years. Important not to wait too long before resorting to massage. When done through the diaphragm, in connection with artificial respiration, it seems to give the patient the best chance for resuscitation. P. Wiart (*Presse méd.*, Oct. 18, 1911).

The older method of exposing the pericardium by creating an opening through the chest-wall is not as ef-

fective as the above unless it be performed as recently pointed out by Babcock.

A new method of cardiac massage. Massage through the thoracic wall as usually practised being time-consuming and requiring the turning back of a flap of the chest, while exposing the patient to the danger of pneumothorax, the writer, to avoid this danger, has suggested a simple method of cardiac massage, using a single finger introduced through a stab wound to the left of the heart. The puncture is made one inch to the left of the sternum in the fourth interspace; the finger instantly pushed through the intercostal space and hooked around the left edge of the heart, which is then intermittently compressed against the overlying sternum. This procedure procured resuscitation in 3 cases. W. Wayne Babcock (*Monthly Cyclopedic and Med. Bull.*, Dec., 1912).

In an unsuccessful case the writer noted that the heart could not be felt through the diaphragm when it was not beating; but as soon as it commenced to beat, the cardiac impulse was much more distinctly felt than the apex beat on the chest wall. The color of the mucous membrane of the lips was restored after 3 to 4 beats of the heart, whereas the color of the peritoneum returned only after a dozen beats. Harries (*Indian Med. Gaz.*, Feb., 1919).

Nor is an opening through the diaphragm an advantage.

Case of a woman of 50 in which the patient's heart and lungs ceased functioning suddenly during a long operation; by prompt massage of the heart, with the hand introduced in the laparotomy wound and squeezing the heart through the diaphragm, the vital functions were restored. The writer found 64 cases of direct massage of the heart in literature. The patients were resuscitated in 2 out of the 20 cases in which the massage was done through the chest-wall and in 11 of the 26 cases in which the



heart was massaged through the diaphragm. None of the patients survived when the hand was introduced through an opening made for it in the diaphragm. The total recoveries thus number 13, or 23.3 per cent. of the cases, but temporary success was obtained in 15 additional cases. He advises incising the epigastrium in five minutes at latest after arrest of the cardiac function and seizing the heart between the thumb and two fingers, to squeeze it rhythmically about sixty times a minute, supplementing this with artificial respiration and insufflation of oxygen if possible. The massage and artificial respiration should be kept up for a time after the first spontaneous movements. It is sufficient to sterilize the field with tincture of iodine, massaging with the gloved hand. Jurasz (Münch. med. Woch., Jan. 10, 1911).

Additional data on this procedure are given in the article on Chest, Surgical Diseases of, this volume.

*Auxiliary Measures.*—**Venesection** is a valuable adjunct in plethoric subjects, especially when **saline solution** and **adrenalin** or **pituitrin** are employed. The essential point seems to be that the veins to be opened should be as large and as near to the heart as possible, in order that the issuing stream of blood be of considerable volume and the relief to the heart as rapid and thorough as possible.

The blood may also be drawn from the jugular vein, when there is reason to believe that distention of the ventricles through the resistance of the blood-column is a factor of the morbid process.

Case of arrest of the heart's action and of respiration during chloroform anesthesia in which the internal jugular vein was opened; compression of the lower chest to relieve the distended right ventricle then re-

sorted to. Several ounces of blood rapidly escaped, and, after the jugular had been clamped by two forceps, artificial respiration was resumed. In less than half a minute the patient made a faint inspiration, followed in a few seconds by another, and, artificial respiration being continued energetically, the heart was heard to beat, at first slowly; but soon the pulse and respirations gained in strength and frequency. The operation was now completed without further administration of an anesthetic. This case is deemed of importance, as demonstrating that the bleeding from the internal jugular vein, by relieving the distention of the right heart, was the main factor in bringing about the recovery of the patient from an apparently hopeless condition. H. F. Waterhouse (Brit. Med. Jour., July 18, 1896).

**Rhythmical traction of the tongue**, introduced by Laborde, is another valuable auxiliary measure which alone has sometimes revived the patient when not too far gone. It consists in seizing the end of the tongue with the fingers, covered with a cloth or the corner of a towel, and then to draw the organ out rhythmically 18 times a minute. This causes the heart, diaphragm, and lungs reflexly to resume their functions in suitable cases.

Laborde's method has been successfully employed in a number of cases. Labbé employed it in a case in which flagellation, artificial respiration, and galvanism had been tried in vain. Verneuil extolled the method, especially when alternated with **flagellations of the epigastrium with a wet cloth**.

The main indication in chloroform accidents is to supply the heart with a non-toxic fluid. **Artificial respiration** will generally answer the purpose

when the trouble is merely arrest of breathing. **Oxygen** is required only exceptionally, but if the heart has stopped beating he advises **venesection**: (1) exposing at once a vein close to the heart and removing 300 Gm. (10 ounces) of blood by pressure on the chest; the vessel is then ligated; (2) keeping up artificial respiration constantly; (3) then injecting slowly, toward the heart, through a needle inserted in an artery on the right side, from 80 to 100 Gm. of tepid **Locke's solution**; (4) then waiting two minutes before doing anything else; (5) then squeezing the heart through the diaphragm, superficially and slowly, not over thirty times a minute, keeping this up for one minute; (6) then waiting for two minutes; (7) giving another injection of Locke's solution (only 60 Gm.) and resuming massage after the fluid has been in the heart for two minutes. This outline of treatment is the only logical method, he thinks, and the success that has been obtained with other methods, he is convinced, was due to the fact that unconsciously some of these principles were followed. His formula for Locke's solution is sodium chloride, 9 Gm.; calcium chloride, 0.2 Gm.; potassium chloride, 0.2 Gm.; sodium carbonate, 0.2 Gm.; glucose, 1 Gm., and distilled water, 1000 c.c. The benefit from this intracardiac lavage has been instructively shown in some recent communications, he states, that of Depage reporting the instantaneous revival of the heart, which forty-five minutes of massage had been unable to accomplish. He warns against too hasty massage, as that would force the non-toxic fluid out of the heart. The aim is to save for the heart the whole benefit of its first effort. Vidal (*Archives gén. de chir.*, Dec., 1910).

Additional auxiliary measures are described in the article on Ether.

**After-effects.**—*Headache, nausea, vomiting, bronchial irritation, and hysterical symptoms* frequently present

themselves after the use of anesthetics, but less so after chloroform than after ether. Symptomatic treatment is only necessary when they persist more than an hour after complete return to consciousness.

When gastric symptoms—*nausea, vomiting, etc.*—prevail, **milk and lime water** frequently succeed in allaying them. If they are stubborn, **lavage** with a lukewarm **solution of carbonate of soda** will usually master them. An hypodermic injection of **morphine**,  $\frac{1}{4}$  grain (0.016 Gm.), with  $\frac{1}{120}$  grain (0.0005 Gm.) of **atropine**, may be used with confidence when the means previously indicated fail. The following combination has been found helpful:

R *Oxalate of cerium*. 2 grs. (0.13 Gm.).  
*Sulphate of cerine* .....  $\frac{1}{2}$  gr. (0.01 Gm.).  
*Calomel* ..... 1 gr. (0.065 Gm.).

M. To make one powder. Three or four powders to be given with intervals of half an hour.

Vomiting after anesthetization is associated with a severe degree of circulatory depression and not infrequently with actual syncope. **Adrenalin** or **pituitrin** injected slowly intramuscularly, 15 minims (1 Gm.) in a hypodermic syringe of saline solution, is indicated.

The value of **hyoscine hydrobromide** in preventing vomiting after chloroform anesthesia was observed quite accidentally by the writer. At his suggestion others have taken it up, all with the happiest results. He gives  $\frac{1}{100}$  grain (0.00065 Gm.) hypodermically as soon as the anesthesia is discontinued. It should be given at once, before sensation returns. In the first case in which it was used the patient had been repeatedly anesthetized, and it had always been followed by severe sickness lasting two or three days. On this occasion,

after the hydrobromide of hyoscine was given there was no illness. J. E. F. Stewart (Australasian Med. Gaz., Sept. 21, 1903).

The value of inhalations of **vinegar** to control nausea and vomiting after chloroform is frequently extolled. According to Lewin, the free chlorine—one of the products of chloroform and which is a marked irritant to the pharyngeal mucous membrane and induces vomiting—is neutralized by the acetic acid. Of 174 cases of vomiting following the administration of chloroform studied by him 125 were relieved by causing them to inhale the fumes of vinegar previously placed upon a towel and left over the face of the patient for a number of hours after the chloroform mask had been removed. If the vomiting returns after this treatment is stopped a renewal of it will be sufficient to check the relapse.

Many early fatalities after chloroform anesthesia are due to the nausea; the closing of the glottis accompanying the retching imprisons in the body an excessive quantity of chloroform; the amount of carbon dioxide is increased, while the amount of oxygen is decreased. The vomiting also weakens the patient. To prevent this, the best course is the following: The patient should be given a **light diet** the day before the operation, consisting for the most part of **peptonized milk**. **Veronal**, **scopolamine**, and **morphine** will reduce the amount of chloroform. Only absolutely pure chloroform should be administered, at 38° C. (100.4° F.). The patient should be kept in an even temperature, and his bed after the operation should be placed in a well-aired room. If there has been much secretion and swallowing of saliva **lavage** should be practised before the patient regains consciousness. But if

vomiting occurs, the patient should drink **albuminous** or **warm water**, **ice cold** or **very hot applications** should be applied to the **stomach**, and an injection of **ergot** or **picrotoxin** should be given. Blanluet (Presse méd., July 7, 1909).

Vomiting being both a cause and a consequence of acidosis, a quart (1000 Gm.) of saline solution by the rectum and retained in the colon is very useful. If the acidosis is marked **sodium carbonate** 2 drams (8 Gm.) should be added to the enema. **Glucose** has also been recommended, given by the mouth or rectum.

The writer **raises** the head end of the **bed** on blocks 12 inches high in all cases after chloroform or ether anesthesia. This he continues for 24 or 36 hours. It results in a great diminution in the tendency to vomiting. Renton (Brit. Med. Jour., Dec. 6, 1913).

There are 2 forms of chloroformic vomiting: One is of psychic origin and benign—only mucus or bile being evacuated. The patients may be obsessed with the idea that they must vomit, or influenced by some association of ideas or be nauseated by the smell of chloroform. The other type of vomiting, the toxic, is produced by the action of some poison on the vomiting center, usually chloroform itself. The patient may be hypersensitive to such toxic influences. Ranking with this type as a serious form of vomiting is that produced by acute postoperative dilatation of the stomach. In toxic vomiting violent accesses may occur without apparent cause, rebellious, frequent, with a peculiar odor of the breath. Slight icterus now appears, with delirium and convulsions and eventually bradycardia. The syndrome is due to the great fragility of the hepatic tissues after chloroform.

The prophylaxis of chloroform vomiting consists in the milk regimen and the use of a purgative. The stomach must remain empty for some 8

hours. This precaution works wonders. The purest and best chloroform must be used. It must have been recently distilled. Much must depend on the anesthetist as some of them hardly ever see vomiting.

After the operation nothing is taken into the stomach for 10 hours when a spoonful of water is first given, then liquid diet, semi-liquid diet, lactovegetarian diet up to full regimen. When *psychic vomiting* appears, a combination of **eucalyptol** and **menthol** is given by the mouth, while **oxygen** is inhaled. Any powerful essence or aromatic substance may be smelled. **Spirit of cologne** inhaled from a mask is a favorite remedy in England. If these measures fail the ordinary substances given to check vomiting may be tested in succession, as **ice**, **charged water**, etc. In *toxic vomiting* the first indication is **gastric lavage**. After a due interval **hot drinks** are given, sweetened or alkalinized, and later milk. Next day a **sodium sulphate** purge is given. If the case is desperate **blood transfusion** is practised. Jeaneney (Gaz. Hebdom. des Sci. Méd. de Bordeaux, Sept. 24, 1916).

*Paralysis* sometimes ensues. It is usually due to pressure against the edge of the table or to strained position of the members. It may arise from the position in which the patient is lying, whereby pressure is exercised upon a supplying nerve, or as a result of tractions on the arm or leg of a violent nature.

**Strychnine** and **electricity** are indicated in such cases, with **massage** calculated to increase the activity of the local circulation.

**POISONING BY CHLOROFORM TAKEN ORALLY.**—Notwithstanding the well-attested lesions produced by the inhalation of an excess of chloroform, the habitual use of the drug, even during a prolonged period, does not always entail severe results.

Case of chloroform addiction of fifteen years' standing in a woman aged 36 years who inhaled from 20 to 30 Gm. (5 drams to 1 ounce) of pure chloroform daily, producing at times deep narcosis. There was no evidence of arteriosclerosis or renal lesions. She suffered from severe hysteria, and had contracted the chloroform habit from using the drug for migraine. There was no tendency to increase the daily dose. There were no withdrawal symptoms when the habit was broken off. Storath (Deut. med. Woch., July 21-28, 1910).

A corresponding quantity taken by the mouth, however, may cause death, preceded by the various phenomena observed in delayed chloroform poisoning (*q.v.*).

Case of a man 28 years of age who was admitted to the hospital in a comatose condition. The afternoon following his admission he became restless and partly delirious. The temperature during the next few days was below normal, after which it gradually ascended, and the patient died of bronchopneumonia. The pathological diagnosis was icterus, pleurisy, and myocarditis, with acute pneumonia, gastric hemorrhages, and nephritis.

The amount of chloroform taken was between 20 and 30 c.c. (5 drams to 1 ounce). Of 47 cases found in the literature of poisoning by chloroform taken internally, 11 died. The writer's animal experiments showed that subnormal temperature and nephritis are the most prominent immediate conditions. Death commonly takes place several days after the administration of the chloroform, and there is found fatty degeneration of the internal organs, especially the liver. H. Ernberg (Nordiskt Med. Arkiv, Feb. 22, 1904).

Two cases of acute chloroform poisoning. The first case was in a man who drank 150 Gm. (5 ounces) of pure chloroform with suicidal intent. Notwithstanding lavage of the stomach with water and milk, saline

infusion, etc., enough chloroform remained to prove fatal in twenty-two hours without recovery of consciousness. As chloroform does not dissolve readily and sinks to the bottom, better results might have been obtained by using oil for lavage. This was emphasized by the writer's second case, that of a man who drank from 80 to 90 Gm. ( $2\frac{1}{2}$  to 3 ounces) of chloroform for insomnia. The writer washed the stomach with warm sesame oil, and then rinsed it with olive oil until there was no odor of chloroform in the stomach content. The lavage was continued for one and a half hours, 7000 c.c. (220 ounces) of oil being used. Owing to asphyxia, artificial respiration had to be resorted to for a time, interrupting the lavage. Withdrawal of 300 c.c. (10 ounces) of blood was followed by saline infusion, and in twenty-four hours the patient was himself again except for a slight headache. He did not complain of the usual chloroform irritation of the digestive tract. The favorable termination in this case is undoubtedly ascribable to the thorough washing out of the stomach with the warm oil until the last trace of chloroform had been removed. Wirth (Wiener klin. Woch., Jan. 14, 1909).

**THERAPEUTICS.**—The morbid effects chloroform awakens in the liver particularly, and which are the source of the condition known as delayed poisoning (reviewed at length in the earlier portion of this article), have restricted its internal use as a therapeutic agent; especially has this been the case since the toxic action of the drug on the tissues, when it is given internally in small doses, has been found to be as marked as when relatively larger doses are administered by inhalation.

Chloroform repeatedly administered by the respiratory passages, subcutaneously, and by the stomach in small doses rapidly kills rabbits.

The liver shows degeneration of the cells sometimes so marked that the whole center of the lobule is broken down into *débris*. The cells in the center of the lobule are early affected; those farther out, later. Fat is always present, generally in large quantities. The kidney suffers to some extent, but relatively more when the chloroform is inhaled than when injected or given by the stomach. Fat is occasionally found in degenerated cells. The spleen shows intense congestion, the sinuses being packed with red blood-corpuscles. Along with the red corpuscles an orange-colored pigment is generally present, which reacts to the stain of iron. A large number of very large phagocytes are present in most cases. The average weight of the spleen was 0.46 Gm. (7 grains) heavier than in the controls when chloroform was inhaled, and 0.59 Gm. (9 grains) and 0.17 Gm. ( $2\frac{1}{2}$  grains) heavier when injected and when given by the stomach, respectively. Degenerative changes were observed in the cardiac muscle. Fat was not observed in any of the hearts examined. Clark (Lancet, Jan. 21, 1911).

Its real value lies in its analgesic and antispasmodic properties when inhaled in small quantities.

The sufferings of labor may be greatly mitigated without danger by a small quantity of chloroform inhaled from a cone just prior to the oncoming pains. The labor is not retarded and the success of the case is not compromised. The aim should not be to produce unconsciousness, but to blunt the sensibility; given in sufficient dose to produce surgical anesthesia, the general relaxation of the uterine tissues produced tends to increase the dangers of hemorrhage. Bedford Brown, however, states that the alterations in the vasomotor system of the pregnant woman enable her to resist the toxic action of chlo-

roform to a greater extent than usual. The drawbacks of chloroform have caused some obstetricians to prefer ether. It is probable that neither is hurtful when used as above stated.

The writer studied the resistance of pregnant animals, comparing the degree of late chloroform poisoning with that of the non-pregnant. Pregnant dogs are susceptible to chloroform administered shortly before delivery or during labor, and show about the same degree of liver injury as normal dogs. Chloroform anesthesia causes no injury to the liver of the fetus nor to any other fetal organ, in spite of the fact that it can be demonstrated to be present in these tissues. It may be used for the few minutes at the end of delivery, but when operative measures are necessary, before or after delivery, it is a dangerous anesthetic and surely capable of producing injury to the liver in the manner recognized in the case of normal persons. Normal and pregnant human beings are equally susceptible to chloroform poisoning; chloroform anesthesia, the gravid period, is capable of causing liver necrosis. Whipple (Jour. Exper. Med., March, 1912).

In **pertussis** inhalations of chloroform sometimes act in a remarkable manner as a calmate. Violent attacks of cough may usually be stopped by pouring a few drops on the hand and holding the latter a few inches under the child's nose. It is also credited with value in chorea, but the almost continuous abnormal movements in this disease render its use inadvisable. It has also been found helpful in **convulsions**, including those of **tetanus**, **puerperal eclampsia**, and **rabies**, the quantity to be inhaled approximating that required for surgical anesthesia.

Both as regards the clinical symptoms and the autopsy findings there

exists a close analogy between the eclamptic toxemia and the postanesthetic poisoning from chloroform. When, therefore, more or less profound anesthesia is required for several hours in recurring eclamptic convulsions, chloroform is contraindicated for fear that the liver, which is already much damaged by the disease, may be subjected to further injury of like character from the chloroform. These considerations have made it seem advisable to abandon the routine use of chloroform for operative work in obstetrics. Wood (Jour. Mich. State Med. Soc., Jan., 1911).

In **renal** and **biliary colic** inhalations of chloroform offer the best source of relief when the suffering is beyond the influence of safe doses of morphine. It is superior to ether in that a much smaller dose is required to relieve the pain, while the after-effects are comparatively *nil*. Its use in a similar way has been lauded in **pulmonary hemorrhage**, a result which seems readily accounted for by the general vascular relaxation induced by the accumulation of blood in the splanchnic area; this entails a process which causes ischemia of the lungs.

Excellent results from the use of chloroform in 19 cases of **pulmonary hemorrhage**. Chloroform acts by lessening the heart action, reducing the blood-pressure, and diminishing the respiratory movement. The writer gives from 2 to 4 c.c. (32 to 64 minims) of chloroform by inhalation. Results should occur within five to ten minutes. At the same time **ammonium chloride** and small doses of **codeine** are given. Fish (Jour. Amer. Med. Assoc., June 12, 1909).

The liniment is very useful for the treatment of **myalgia**, **lumbago**, **sciatica**, and kindred disorders of rheumatic origin. It is also considerably

employed on the painful areas of acute gout. It has also been tried as antiseptic.

In the treatment of **pus pockets** and **infected wounds**, the writer recommends injections of a mixture of oxygen gas with chloroform and alcohol vapors. The mixture is introduced, after free surgical exposure, through one or several sterilized rubber tubes. Under this measure, suppurative discharge is rapidly lessened and the wounds assume a bright red coloration. The chloroform seems to enhance the leucocytic reaction against the infection, while the oxygen activates hemostasis. Cabanes (*Presse méd.*, Jan. 10, 1918).

#### A. C. E. MIXTURE.

A. C. E. mixture is an anesthetic proposed by Harley (as modified by Martindale), and composed of alcohol, as a menstruum, 1 part; chloroform, 2 parts; and ether, 3 parts; by bulk. It is termed the "A. C. E. mixture" from the initial letters of the names of its ingredients. It is thought to present many advantages over ether or chloroform, and to be less dangerous than chloroform alone and more speedy in its action than ether.

**Administration.**—The A. C. E. mixture does not seem to possess the advantages claimed for it. While entailing the dangers of chloroform anesthesia, it tends to cause confusion in the recognition of the danger signals.

The fact that chloroform is not as safe an anesthetic for children as was generally thought to be the case, has caused the A. C. E. mixture to be tried as a substitute, but only for the first stage, ether being then substituted.

**Physiological Action.**—Truman has shown that the removal of the de-

pressing action of the chloroform upon the heart by the stimulating action of the ether is not based upon chemical facts, the latter vaporizing out of all proportion to the chloroform. In administering the mixed anesthetics, therefore, a vapor of varying and uncertain composition is employed, which does not prevent the morbid effects of either drug.

**Untoward Effects.**—The deaths occurring after the administration of the A. C. E. mixture seem to be associated with pathological conditions similar to those met with in fatal cases following the use of chloroform.

#### C. E. MIXTURE.

A mixture of chloroform and ether has been credited with greater safety than either of these two agents. The best results are obtained by using a mixture of 1 part chloroform to 9 parts of ether, using a drop-bottle to administer it. The period of excitation is said to be shortened, the frequency of syncope lessened, and post-operative sickness reduced in intensity and frequency of occurrence.

The mixture of chloroform and ether believed to be the best anesthetic to use during the course of **pregnancy**, while it is very good for the operation for the **removal of tonsils** and **adenoids** in children, especially those under 4 to 5 years of age. In the operation for amputation of the breast, when the stage is reached just prior to the actual removal of the organ, and shock is so liable to take place, C. E. proves most serviceable. Obese patients and the aged take this anesthetic well. Patients who are weak and wasted by disease take this mixture better than healthy, strong, and vigorous individuals, but this applies to every anesthetic. L. Erasmus Ellis (*Clinical Jour.*, Sept. 9, 1908).

**C. O. MIXTURE.**

This combination of chloroform and oxygen has for its purpose the prevention of asphyxia. A few inspirations cause the appearance of a glow on the patient's face, the anemic appearing perfectly healthy. The period of surgical narcosis is said to be reached promptly. The respiration and pulse rate remain uniform but slow.

In a personal experience with the C. O. mixture (introduced by the writer) comprising more than 300 cases, 166 patients were fully conscious immediately after operation; 13 required between 8 and 30 minutes; one woman, after the use of 55 Gm. (1¾ ounces) of chloroform, slept 3 hours; 21 dispensary patients got off the table and walked home. Wohlgemuth (*Interstate Med. Jour.*, Oct., 1901).

The writer records the favorable views of a number of prominent surgeons, and reports 2000 cases of his own in which not the slightest difficulty or annoyance arose. An advantage of the CO method lies in the exact dosage which is possible. The writer believes that the oxygen acts as an antidote to the chloroform. Roth (*Zentralbl. f. Chir.*, Jan. 7, 1905).

Experimental researches by the writer suggests that chloroform given with oxygen is much less toxic than when given with air; but even at best, enough toxicity is left to compel caution. The ideal general anesthesia to date is that induced with ether, possibly preceded by morphine, with only enough chloroform, in small amounts, to render the anesthesia more profound. Lenge-mann (*Mitt. a. d. Grenz. d. Med. u. Chir.*, 3d Suppl. No., 1907).

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**CHLOROSIS.—DEFINITION.—**

A form of anemia exclusively affecting females, and characterized pathologically by serous plethora with striking hemoglobin deficiency of the erythrocytes, and clinically by a peculiar type of pallor and by symptoms referable chiefly to the cardiovascular, generative, and digestive systems.

The writer recalled the fact that chlorosis is now believed to involve the entire organism, and to be actually a basic anomaly of the latter, which in turn almost necessarily implies a disturbance of the organs of internal secretion. In support of this he deems it significant that the serum from 18 girls with chlorosis regularly digested ovary and uterus tissue when the dialysis test was applied and did not digest other tissues. Schmidt (*Münch. med. Woch.*, June 16, 1914).

**SYMPTOMS.**—Chlorosis develops slowly and insidiously, ultimately, if unchecked, giving rise to a most distinctive group of symptoms, of which, in the typical example of the disease, the objective are by far the more conspicuous. Of the subjective phenomena, dyspnea is unquestionably the most constant and most formidable symptom to be dealt with. In some cases it amounts merely to a moderate shortness of breath provoked by undue exertion, but in others it takes the form of an habitual breathlessness, which, from even trivial bodily or mental stress, may become most distressing and alarming to the sufferer. Cardiac palpitation, almost as common a complaint as dyspnea, is a most annoying associated symptom. Languor, generally becoming steadily more marked as the disease matures, is another symptom of great significance, and in the extreme case the indisposition sometimes amounts to almost complete muscular debility



and incompetence. Venous thrombosis is a grave complication which supervenes in not more than about 2 per cent. of cases, most frequently implicating the femoral vein. Phlebitis of the legs, though uncommon in the average case, may develop as a complication of considerable moment.

In reporting a case of chlorosis with thrombosis of the subclavian vein, the writer states that thrombosis of the lower extremities occurs usually in the femoral and iliac veins and almost always there is some extension into the inferior vena cava. Cases of this kind have been reported by Batle, Lowenberg, and Huels. Batle tells of a young chlorotic girl who was afflicted with a phlebitis of both femoral veins and of the inferior vena cava with consequent enormous enlargement of the veins of the abdomen. Simultaneously there occurred pains in the head, vomiting, and coma. Autopsy showed thrombosis of the inferior vena cava, common iliac veins, and superior longitudinal sinus. E. A. Rogers (Boston Med. and Surg. Jour., Sept. 17, 1912).

A disturbed digestion is common in the chlorotic subject, whose coated tongue, heavy breath, flatulence, and abdominal discomfort point to a derangement of the gastrointestinal functions. In about one-half of all cases there is stubborn constipation. As complications affecting the stomach, dilatation, dislocation, and ulceration are to be borne in mind. The appetite is likely to become extremely variable and capricious: voracious hunger may alternate with complete anorexia, and a curious perversion of taste frequently makes its appearance—one girl may evince an insatiable longing for sour and highly spiced foods; another, for quantities of sweets, or for materials such as chalk, slate, and clayey substances. Arneth observed extreme hyperacidity.

Though reputed to be a fertile class, chlorotics are peculiarly prone to amenorrhea, or if not affected with a total suppression of the menses they are likely to flow scantily, irregularly, and perhaps painfully. Chlorosis antedating menstruation is generally regarded as more intractable than chlorosis appearing after this function is established. In a fair percentage of cases menorrhagia has been noted, and in some the discharge is abundantly leucorrhœal. Menstrual disturbances, then, are so common in chlorosis as to constitute one of its most prominent symptom groups.

Most chlorotic girls show more or less pronounced nervous symptoms, which ordinarily betoken nothing more serious than an underlying neurasthenia due in all probability to the deleterious effects of faulty oxidation. Thus, one is prepared to meet with irritable dispositions, perverted wills, unreasonable caprices, and petty temper, or one may encounter mental apathy, lack of concentration, unnatural drowsiness (or, it may be, distressing insomnia) on the part of the patient. Gastralgia, cardialgia, and neuralgias, especially of the face, also are common complaints. Optic neuritis and peripheral neuritis are to be recalled as possible, but, fortunately, improbable nervous lesions that may supervene in chlorosis.

Pallor and plumpness form a striking combination of objective symptoms in the typical example of chlorosis. The pallor sometimes conforms to the traditional light-olive hue so generally ascribed to "green sickness," but more often the skin is stained a faint yellowish tint, or it may have the appearance of alabaster. Blanched mucosa, snow-white finger-nails, and inordinately blue veins corroborate the significance of

these other integumentary signs. In contrast to the foregoing, certain chlorotics have considerable color, as in those designated by the term "chlorosis rubra" or "florida." The plump, well-nourished appearance of most chlorotic girls is attributable chiefly to a retention of subcutaneous fat, but it may be, however, due in part to edematous swelling of the cellular tissues. Unnatural fullness of the superficial vessels, tumultuous arterial throbbing, and venous pulsation in the neck are noteworthy visual findings in many instances, and Joffroy's sign (absence of cutaneous wrinkling of the forehead and immobility of the eyebrows when the patient glances upward without moving the head) is observed not infrequently, as in Basedow's disease. Cardiovascular murmurs, generally audible most distinctly at the base of the heart, are important auscultatory signs in chlorosis, as also are the venous murmurs, heard over the veins of the neck, and ordinarily referred to as the "humming top murmur," *bruit de diable*, and *Vencensause*. There may be actual enlargement of the heart, or fictitious enlargement, due to bilateral retraction of the anterior pulmonary borders. The pulse is likely to be unduly rapid, and its rate and rhythm are extremely unstable; the vessels, though overfull, are probably not subject to hypertension.

Although there are many subjective symptoms of chlorosis, it is comparatively seldom that structural changes occur in the fundi, just as it is rare to see extensive histological changes throughout the body the direct result of this disease. Thus, in 19 cases of marked chlorosis examined by the writer and reported by him in 1897, appreciable swelling of the disk or true neuritis was not present in any instance, though a slight obscuration

of the edges of the disk with broadening and some pallor of the retinal veins occurred in quite a number. Of 50 chlorotics examined by Saundby and Eales in 1882, however, some degree of neuroretinitis was found in 8 per cent. In addition to these slight degrees of neuroretinitis, chlorosis at times evokes a most intense inflammation of the optic nerve and surrounding retina, and a number of cases have been recorded in which the changes in the fundi were so marked that they were mistaken for the ocular inflammations of albuminuria and of brain tumor. The writer has recently had a case of this intense form of neuroretinitis due to chlorosis under his care at the Wills Eye Hospital. A few days after admission, both eyes were the seat of an intense neuroretinitis, that of the right eye being accompanied by great edema of the retina. The veins in both eyes were enormously distended, while the arteries in the right were much reduced in size. The arteries in the left eye were of about normal caliber. Both veins and arteries were tortuous, especially the former. No spontaneous venous or arterial pulse was demonstrable or could be elicited by pressure. The veins were dark and full and hidden in places by the swollen retina. There were no hemorrhages or isolated areas of extravasation in either eye, save for a small, round, fluffy area of extravasation in the retina of the right eye far in the periphery in close association with the inferior temporal vein. The swollen veins could be followed into the periphery of the retina, but the arteries in the right eye gradually faded away, some 2 or 3 disk diameters from the papilla. The fields in both eyes were somewhat concentrically contracted; that of the left eye was free from scotoma, while a large absolute scotoma extended 20 degrees from fixation upward and outward in the right eye.

Hirschberg was the first (in 1879) to note the occurrence of optic neuritis in chlorosis. Other cases were

reported shortly after this, however, by Bitsch, Gowers, Williams, Mackenzie, Schmidt, Dieballa, and others, so that there are now about 20 fully recorded cases in the literature. Wm. Campbell Posey (Transactions of the Amer. Ophthal. Soc., 1909).

The *blood-picture* of chlorosis is in no sense characteristic, for precisely similar changes may occur in various forms of secondary anemia, notably in those consequent to syphilis, malignant disease, sepsis, nephritis, and tuberculosis. A strikingly disproportionate oligochromemia is perhaps the most noteworthy feature of the chlorotic blood-picture, which generally shows hemoglobin figures ranging between 40 and 50 per cent. of normal, and in some instances as low as 20 per cent. or even less. The erythrocytes also suffer, but their diminution is much less, relatively, than that of the hemoglobin, in view of which a low color index (indicating the individual richness of each cell in hemoglobin) is the usual finding. In a series of 155 consecutive cases of chlorosis the writer found these average values: hemoglobin, 46.8 per cent.; erythrocytes, 3,816,486 per c.mm.; leucocytes, 6457 per c.mm. Beyond a prevalence of pale, undersized erythrocytes (microcytosis; achromacytosis), the structural changes affecting these cells are of little consequence, though in severe cases an occasional normoblast and a few distorted poikilocytes are sometimes demonstrable.

The leucocyte formula remains virtually normal, save for the somewhat constant occurrence of a large-celled relative lymphocytosis at the expense of the neutrophilic and the eosinophilic leucocytes. The total leucocyte count does not deviate from the standard of health, except in the face of such com-

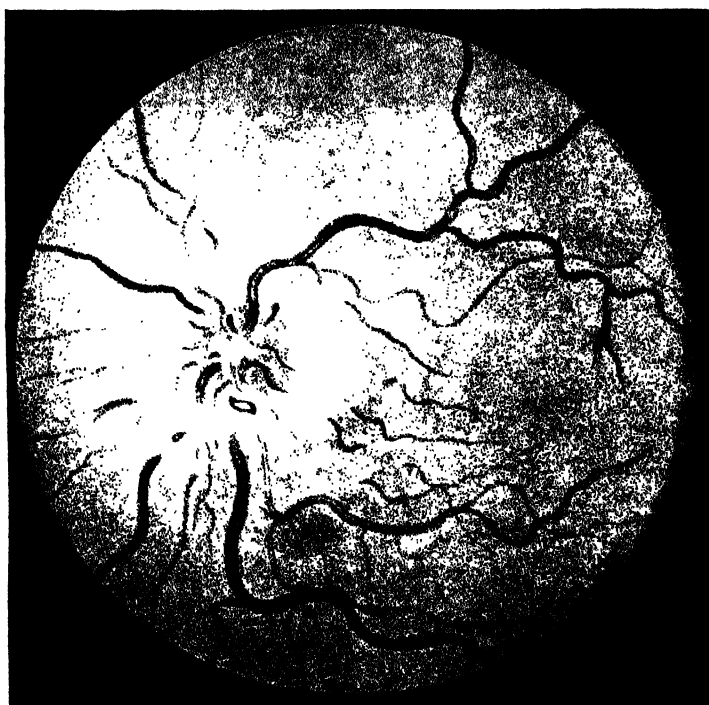
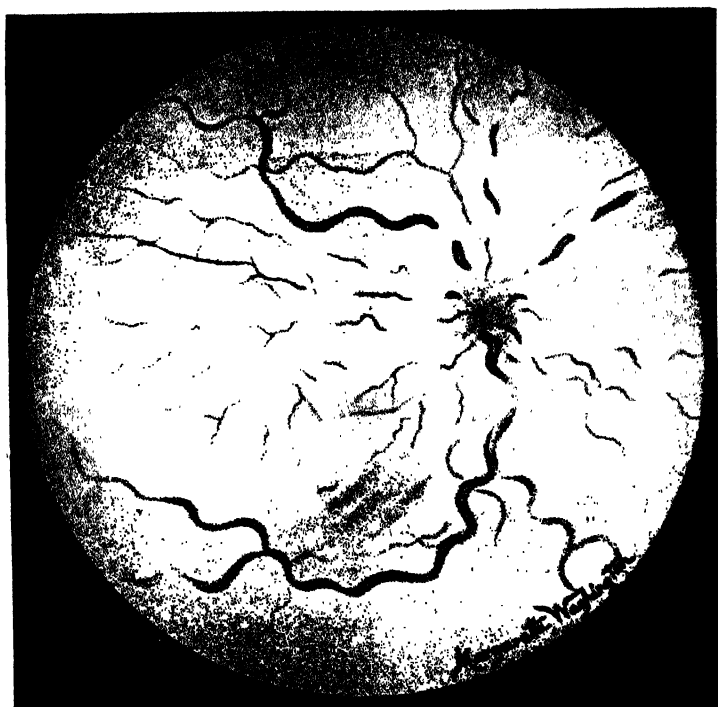
plications as may cause either leucopenia or leucocytosis.

**DIAGNOSIS.**—The direct diagnosis of chlorosis rests upon a blood-picture of disproportionate hemoglobin loss plus the characteristic chlorotic phenomena enumerated above. Without these latter findings, it must needs be emphasized a diagnosis of chlorosis is never justified, for the disease can by no means be recognized merely by the detection of oligochromemia and a low color index.

*Pernicious anemia*, aside from having a much graver group of symptoms, is distinguishable from chlorosis by its intense anemia of the so-called megaloblastic type, *i.e.*, one characterized by extremely low erythrocyte values, relatively less hemoglobin losses, high color indices, and structural changes indicating embryonal reversion of the bone-marrow—large (fetal) nucleated red corpuscles and giant non-nucleated cells of the same type.

*Incipient tuberculosis* has been often mistaken for chlorosis, owing to the similarity of the blood changes in the two conditions, but doubts on this score can be easily settled by a careful analysis of all the available data, bedside and laboratory, of the case in question. This comment also is applicable to the differentiation of *syphilis*, *nephritis*, and certain other disorders which sometimes superficially resemble chlorosis.

**ETIOLOGY.**—Perhaps the most alluring theory to explain the genesis of chlorosis is that of Lloyd-Jones, who believes that the affection is excited by an excessive outpouring of an internal (ovarian) secretion at or about the time of the subject's first menstruation. This author, moreover, points out that chlorotic girls generally belong to large



Intense Neuroretinitis in Chlorosis. (*Posey.*)  
Transactions of the American Ophthalmological Society.



families, and he insists that blood of the chlorotic type (*v. infra*) is an indication of great fertility. Bunge's hypothesis, quite disproved by Stockman, assumes that chlorosis arises from the presence of sulphureted hydrogen in the bowel, whereby the ingested organic food-iron is changed into an inorganic insoluble sulphide, which, remaining unabsorbed, cannot be utilized as a source of iron manufacture by the organism. Other reputed, but unproved causes of chlorosis include intestinal autointoxication consequent to habitual constipation (Andrew Clark); tight stays (Rosenbach); hemolysis from toxins generated by gastrectasis (Pick), and mesoblastic hypoplasia, or congenitally arrested development of the arterial system (Virchow). Despite the plausibility of these different hypotheses, none of them is entirely convincing, in view of which the exact origin of chlorosis, in the light of our present knowledge, must remain a hematologic mystery.

There is much to sustain the assumption that chlorosis is a special form of defective formation of blood resulting from the fact that the female genital apparatus acts on the nerve-centers presiding over the production of blood. The genitals are frequently infantile, but may develop later. Out of 85 sterile women examined, 56 stated that they had had chlorosis during their girlhood. The belief that chlorosis is a neurosis seems to indicate a direct mediation of the nervous system as well as of the internal secretions. The signs of temporary eunuchoid conditions, sometimes observed in boys just before puberty, are generally found in families in which the girls present chlorosis. The boys develop the transverse roll of fat above the symphysis and their skin becomes like that of a girl, all of which in time they outgrow. The transient obesity

is probably due to defective thyroid functioning at this time, owing to the lack of sufficient interstitial tissue in the testicles. He has frequently encountered in late years a condition suggesting chlorosis in some points and yet in others directly opposite. Young girls previously entirely healthy cease to menstruate after some acute infectious disease; they lose appetite and weight and look old, while trophic disturbances are noted in the skin and fingers. In 3 such patients there was considerable scleroderma. The blood does not suggest chlorosis, but rather polycythemia. C. von Noorden (Med. Klinik, Jan. 2, 1910).

Of the numerous predisposing factors of chlorosis, sex is by all odds the most important, inasmuch as the disease is confined to females, usually those beginning or passing through the adolescent period of life. Those instances of chlorosis occasionally met with in more mature women are most likely relapses of an initial attack during earlier life. Male chlorosis, so-called, is a medical myth. Heredity is also an interesting etiologic factor, and it is generally admitted that the affection is peculiarly prone to attack certain families. Albutt emphasizes this fact by relating his experience of seeing "in family after family . . . the daughters, one after another, as they arrive at puberty, coming for aid in the disorder for which I formerly treated their mothers."

As contributory, but by no means direct factors of chlorosis underfeeding and overwork, defective hygiene and insufficient exercise, malnutrition and gastrointestinal disorders, mental stress and nostalgia are to be given due weight. Hospital statistics tend to show the special frequency of chlorosis among domestic servants and newly arrived immigrant girls.

The family history of 36 cases of chlorosis studied during the last five years to ascertain the connection between chlorosis and tuberculosis. In 1890 Jolly concluded from an examination of 54 cases that in the majority of instances personal or family history of scrofula or tuberculosis was to be found. The 36 cases now recorded, however, show that tuberculosis has not any more influence in the causation of chlorosis than have other pathological states. The influence of hereditary tuberculosis is only exerted by enfeebling the stock. Leclerc and Levet (*Lyon méd.*, Aug. 4, 1901).

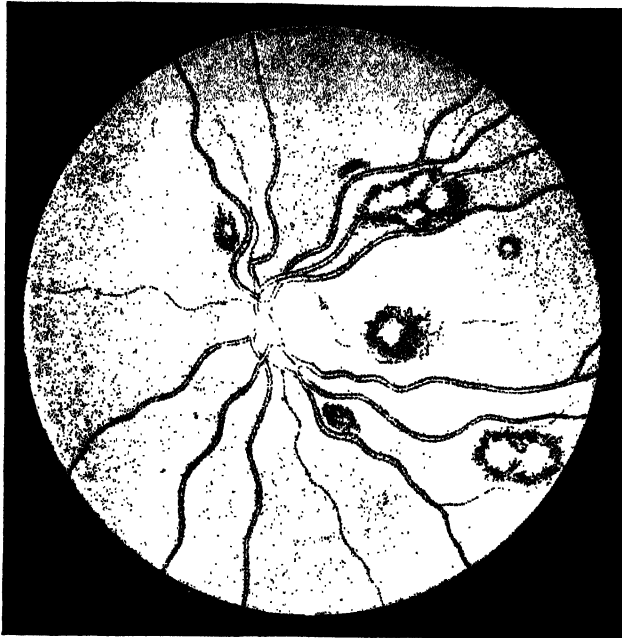
As taught by Landouzy, a truly chlorotic patient is either tuberculous, syphilitic, nephritic, gastropathic, or attacked with some disease likely to cause anemia. Symptomatic anemias differ in no way from chlorosis. Of all the causes of an anemia likely to give rise to an apparent chlorosis, none is more important or more frequent than tuberculosis. Labbé (*Presse méd.*, Aug. 31, 1904).

In the writer's cases it was not so much the subjective symptoms found in light chlorosis and neurasthenia, such as exhaustion in the morning, lack of desire for exertion, slight headache, as the striking pallor of the face and mucous membranes which led him to suspect chlorosis. In most of the cases he found a systolic murmur in the heart and accentuated pulmonic second sound. The blood examination always showed the normal number of red blood-corpuscles, and hemoglobin from 90 to 95 per cent. In all the cases treatment with iron was followed by the best results, relieving not only the subjective symptoms, but causing a disappearance of the pallor. He agrees with Morawitz in calling those cases chlorosis with a normal hemoglobin percentage, but an increase in the entire blood quantity. Almost all of his patients gave a history of masturbation or interrupted coitus. Since almost all authorities mention the genital functions in relation to chlo-

rosis, he believes that this association is important, especially so since most of the before-mentioned symptoms of chlorosis are found in cases of masturbation in young men. Paul Groag (*Münch. med. Woch.*, Bd. lvii, S. 1596, 1910).

The writer applies the tuberculin test in every case of persisting chlorosis, and states that a positive response was obtained in 74.8 per cent. of 55 cases in which there was nothing otherwise to suggest the existence of tuberculosis. This finding confirms his assumption that tuberculosis is responsible for the chlorosis in a surprisingly large number of cases. The reaction was obtained with 5 mg. or less in all but 5 of the patients. In 48 other cases the chlorosis accompanied manifest signs of tuberculosis. In the tuberculous cases in which the chlorosis was the first or one of the first manifestations of the infection, the patients reacted to the tuberculin test with smaller dosage and in a larger percentage than the rest of the tuberculosis suspects, and the percentage of negative responses was less. Zickgraf (*Fortschritte der Med.*, May 12, 1910).

While it may appear plausible at first sight to offer tuberculosis as a cause for chlorosis, such a relationship still lacks satisfactory proof. In a large number of cases of chlorosis tuberculosis can be reasonably excluded. Most of the cases that have been followed up in after-years remain free from tuberculosis, but the available records of these cases are few. While the two diseases share common symptoms, there is usually a marked difference in their relative intensity, and in many instances prominent symptoms of one affection are lacking in the other. Specially worthy of note is the common occurrence in chlorosis of a hemoglobin percentage below 70, while tuberculosis usually shows a percentage above this. Of distinct significance is the action of iron, which behaves as a specific in chlo-



Appearance of the Fundus in Two Cases of Chlorosis. (*C. A. Oliver.*)

Transactions of the American Ophthalmological Society of 1897.





rosis, often producing, even in the absence of other treatment, rapid and marked curative effects, far more striking than the effects ordinarily following the use of the same drug in tuberculosis. Cases in which the chloranemia can be traced to tuberculosis should not be regarded as cases of chlorosis. C. M. Montgomery (*Med. Record*, Oct. 5, 1912).

**PATHOLOGY.**—Apart from the blood changes elsewhere mentioned, little is known of the pathologic changes incident to chlorosis, owing to the meagerness of autopsy data relating to this condition. In certain cases there has been discovered a curious underdevelopment of the arterial system, the basis of Virchow's uncorroborated "hypoblastic hypothesis" of chlorosis, but characteristic changes in the internal viscera have not been described, though in severe cases structural damage common to any high-grade anemia may supervene—myocardial degeneration, cardiac dilatation, fatty metamorphosis of the arterial media, and general pallor of the internal organs. In a single autopsy Grawitz could determine no definite marrow changes. Enlargement of the spleen, unnatural vascular swelling of the thyroid gland, gastrectasis, and gastropnoia are among the numerous other findings, in no wise constant nor distinctive, which have been ascribed to the chlorotic state.

It is of interest here to refer to Lloyd-Jones's elaborate studies, which prove that the specific gravity of the whole blood is diminished in direct relation to the losses of hemoglobin and red corpuscles; that the specific gravity of the plasma remains unaltered or, indeed, may be in excess of normal, and that the specific gravity of the serum is virtually not affected. To Haldane and Lorrain Smith we owe the proof

that chlorotics are subject to a true serous plethora, due to a substantial excess of blood-plasma. Extravascular coagulation of the blood is abnormally slow, and the clot is deficient in fibrin.

**TREATMENT.**—Rarely does a chlorotic fail to become well under a proper course of treatment, consisting of the administration of iron, supplemented by rest, a liberal diet, fresh air, and sunshine. *Blaud's pill*, with or without *cascara*, cannot be improved upon, despite the vogue in certain quarters of the numerous proprietary organic irons.

There are marked cases of chlorosis in which the condition of the blood is normal, or nearly so. Such cases are not rare. The influence of iron is just as favorable in these cases as in those associated with distinct anemia. Anemia is therefore not the cardinal symptom of chlorosis, but only one symptom among others. The disturbances of menstruation, venous murmurs, water retentions, and the majority of the subjective symptoms met with in chlorosis are not always dependent on an anemia. It is improbable that the curative action of iron in chlorosis is to be ascribed to a stimulative effect upon the blood-forming organs, in particular to a stimulative effect upon the formation of hemoglobin. The uselessness of iron in almost all non-chlorotic anemias, as compared with arsenic aside from other observations, is an evidence against the existence of such a stimulative action. The point of attack of the iron in chlorosis is to be sought not in the blood-forming organs alone, but also in the as yet unknown root of the disease. Morawitz (*Münch. med. Woch.*, July 5, 1910).

Comparative results obtained by the writer in 33 cases of chlorosis. Thirteen were treated with arsenic alone, 12 with iron only; the remain-

ing 8 were given both iron and arsenic. Arsenic was used in the form of arsenous acid in doses of from 0.005 to 0.01 Gm. ( $\frac{1}{2}$  to  $\frac{1}{6}$  grain) a day either in pill form or by subcutaneous injection. The patients treated with arsenic alone derived little or no benefit. The hemoglobin percentage after two or three weeks of this treatment increased slightly, but there was an actual fall in the number of red blood-cells. In addition to this lack of improvement, untoward symptoms frequently occurred from the use of the arsenic. Consequently, arsenic alone has no therapeutic effect upon chlorosis. Iron alone was given in the form of a modified Blaud pill for four weeks. The hemoglobin percentage increased markedly and the number of red blood-cells rose to nearly normal. The average of 49 per cent. hemoglobin rose to 87 per cent. and the number of red blood-cells increased from 4,000,000 to 5,000,000. The patients treated with iron and arsenic in combination received in addition to the Blaud pill an average dose of 0.006 Gm. of arsenous acid a day. After four weeks of this combined treatment the average hemoglobin percentage rose from 37 to 96 per cent., and the red blood-cells increased from 3,000,000 to 5,100,000. This combination of **iron and arsenic** has a more rapid and more complete curative action than iron alone. Seiler (*Deut. med. Woch.*, Bd. xxxvii, S. 1340, 1911).

The treatment of chlorosis with arsenic in the form of **arsenous acid** does not cause an increase of the hemoglobin nor of the number of red blood-cells. But its treatment with iron in the form of **Blaud's pills** results in a rapid increase of the hemoglobin and when the blood-cells are diminished, an increase in their number. This regeneration of the hemoglobin and of the red blood-cells is not rapid as measured by the single weeks. The treatment of chlorosis with **iron and arsenic** combined gives a definitely increased improvement in

comparison to the results obtained by the treatment of chlorosis with iron alone. The increase of the hemoglobin occurs more rapidly, and the number of red blood-cells shows an increase of two or three times that obtained when iron alone is used. The arsenic is given in the form of arsenous acid, in doses of from 0.002 to 0.003 Gm. ( $\frac{1}{32}$  to  $\frac{1}{20}$  grain) three times a day. These doses are combined with the ordinary doses of iron. Zwetkoff (*Zeit. f. Exper. Path. u. Therap.*, Bd. ix, S. 393, 1911).

**Iron** has the power of carrying oxygen and then of liberating it as a direct oxidase. It also stimulates the action of the diastases and organic catalytic action. It is absorbed into the hemoglobin molecule, and helps to reconstitute the blood-cells. Since the liver plays an important part in the genesis of blood, no result can be expected from the free use of iron unless this organ is in a healthy state and free from degeneration or fatty conditions. The liver must be carefully examined before iron is prescribed. In cases where the function of the liver is sluggish, the administration of iron will stimulate it to act. Robin (*La Clinique*, May 26, 1911).

The writer attributes chlorosis to torpid blood formation, which differs in degree in different cases. **Iron**, when given in sufficient doses, acts as a stimulant, particularly of the bone marrow. In this it excites a stormy reaction, which causes quantities of young elements to be thrown into the blood. Not only the hemoglobin elements, but the whole of the bone marrow appears to be stimulated. Naegeli (*Schweizer. med. Woch.*, July 29, 1920).

The average case is most benefited by a course of three pills of iron daily for the first week; six pills daily for the second week, and nine pills daily for the third week, beyond which limit it is scarcely ever necessary to go. If iron given by the mouth causes gastric disturbances, the metal may be given sub-

cutaneously, as advised by J. L. Morse, who uses the **citrate of iron** in  $\frac{3}{4}$ -grain doses, with gratifying results, in the treatment of so-called "chloroanemia" in young children. Owing to the frequency of incomplete cures (most of them masquerading as "relapses"), small doses of iron should be administered to the patient for several weeks after the normal blood-picture is attained.

**Hot baths** have a powerful stimulating action on the bone-marrow. In chlorosis the writer orders a bath with the water constantly at 40° C. (104° F.) taken about 11 A.M. for ten to twenty minutes. The patient then takes a **cold douche** and is rubbed down and then lies down for an hour. Three of these baths are taken during the week for from four to six weeks. A cool wet cloth is kept on the head during the bath. In a month, he declares, the improvement generally amounts to a complete cure. Rosin (*Therapie der Gegenwart*, Bd. xlvii, Nu. 7, 1906).

One medicament is of great value in chlorosis: **calomel** in tonic doses—not cathartic doses—that is, from  $\frac{1}{30}$  to  $\frac{1}{30}$  grain (0.0013 to 0.0022 Gm.), given three times a day, but not oftener. Bridge (*Jour. Amer. Med. Assoc.*, Aug. 24, 1907).

Twelve cases of chlorosis in which the writer supplemented **iron tonics** with **hot baths** to induce sweating and thus stimulate the general metabolism and blood production. The sweating seems to mobilize the deposits of iron in the organism. The metabolic findings, as he tabulates them for each of his cases, confirm the efficacy of this method. Ferrario (*Gaz. degli ospedali*, Aug. 12, 1909).

Many cases do well on an occasional **saline laxative**, in addition to their iron treatment, or **lactic acid milk** or **B-naphthol** may be given, in the hope of keeping the intestines

relatively clean. The chlorotic subject must eat heartily of **red meats**, of **eggs**, and of **green vegetables**, and she should drink moderate quantities of **pure milk**, provided that it causes neither constipation nor indigestion. **Absolute rest in bed** until the hemoglobin percentage approaches the normal standard must be insisted upon as an essential for a rapid and permanent cure.

The restriction to vegetable food is distinctly harmful in chlorosis; the patient needs about 100 or 120 Gm. (3 or 4 ounces) of albumin daily, preferably in the form of meat, and best ingested at breakfast.

Chlorotic girls generally breathe superficially. Continued **systematic breathing exercises** will improve the ability to walk and climb stairs, etc., long before the blood shows any decided change for the better. The constipation that follows the use of iron may be due to too great reliance on the rectal syringe. Constipation from stagnation above the rectum can be cured by dietetic measures without fail, but, when the rectum has been trained to sluggish action from too frequent use of the syringe to promote defecation, conditions are far less favorable for a cure. This is almost the sole cause of obstinate rectal constipation.

The writer has found **iron mineral waters** a great deal more beneficial and less liable to induce constipation than pharmacopeial iron, and also that arsenic in the form of an **arsenical water** is better tolerated than in any drug preparation.

Both iron and arsenic act especially by stimulating the blood-producing apparatus, which re-enforces the too feeble excitation from the ovaries. C. von Noorden (*Med. Klinik*, Jan. 2, 1910).

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**CHOKED DISK.** See OPTIC NERVE AND RETINA: OPTIC NEURITIS OR CHOKED DISK.

**CHOLANGITIS AND CHOLECYSTITIS.** See LIVER AND GALL-BLADDER, DISEASES OF.

## **CHOLELITHIASIS: GALL-STONE DISEASE.**

[**History.**—Curiously enough nothing is mentioned in the historic medical records that are preserved from antiquity and from the middle ages—of gall-stones. Antonius Benivenius (died 1582) was the first to describe their occurrence in the findings of an autopsy on a woman who died after intense pains over the hepatic region. The stones are described as in and alongside the gall-bladder, which is evidence of a perforation.

A very good clinical history of gall-stone disease is given by Fernel in 1554. He knows that with obstruction of the ductus choledochus a swelling of the gall-bladder occurs, the feces turn white, the urine very dark, but during occlusion of the hepatic duct he describes the gall-bladder as empty.

The great anatomist Glisson (1569) gives a true account of hepatic colic associated with icterus and about the same time Blasius pictures the first exactly observed cases of abscess formation as a consequence of gall-stones. Sydenham's descriptions are disappointing, for he conceives hepatic colic to be only a hysterical sign and does not mention gall-stones. A very exhaustive and true description is presented by Friedrich Hoffmann, who attributes the stone formation to stagnation of the bile.

During the second half of the eighteenth century a clearer insight into the nature of cholelithiasis is revealed, especially in Morgagni's great work, "*De Sedibus et Causis Morborum*," but also the experimental and anatomical studies of Haller, Fourcroy, and Vicq d'Azyr threw a new light on these biliary abnormalities.

In the nineteenth century the clinical conceptions of cholelithiasis were broadened by Andral, Trousseau, Frerichs, and others, and since the evolution of physiological chemistry Naunyn has written a

masterly presentation and *résumé* of the entire knowledge up to his time (see Naunyn, "*Die Entwicklung d. neuen Medicin*," etc., im 19 Jahrhundert, Jena, 1900; also Penzoldt and Stintzing's "*Handbuch*," etc.; v. Leyden's "*Handb. d. Ernährungstherapie*"; Eulenburg's "*Real Encycloped.*," and Nothnagel's composite work).

It should be stated, however, that when S. Th. Sömmering wrote his "*De Concrementis Biliaris Corporis Humani*" in 1795 he could cite 213 authors who had written on gall-stones, among which were 15 works with illustrations.

Since Mignot in 1898 succeeded in producing gall-stones by injection of bacteria the virulence of which had been reduced, the doubt that this was a bacterial infection in most cases of cholelithiasis was removed. I must state, as a matter of historic accuracy, that my colleague Dr. Charles W. Mitchell found typhoid bacilli in the gall-bladder and in a small soft area in the center of a gall-stone in 1897.

The surgery of cholelithiasis was developed especially by the following: in America by J. Marion Sims, in Germany by Kehr and Langenbeck, in France by Courvoisier, and in Switzerland by Kocher. J. C. HEMMETER.]

**SYMPTOMS.**—When such do occur they are at first very indefinite; general distress and slight pains in the region of the liver, digestive disturbances, and slight icterus are among the first symptoms and signs; but their dependence upon gall-stones is not always recognized in time. It is very rare that one is able to palpate the gall-bladder in individuals with thin abdominal wall. On the whole, it may be stated that gall-stones can in rare instances be felt.

[The names of Courvoisier and Cruveilhier are occasionally confused in the studies on cholelithiasis. Léon Baptiste Cruveilhier (1791-1876) was professor of pathological anatomy in Paris and enriched medical science with brilliant contributions to the pathology of the liver. Among other things he states that con-

stricted liver and gall-bladder frequently go together (see Nothnagel System, Bd. xviii, S. 200). Courvoisier (Statistische Beitr. z. Path. u. Chir. d. Gallenwege, Leipzig, 1890) states that a distinctly palpable gall-bladder in the course of cholelithiasis is absent in 84 per cent. and present in 16 per cent. of the cases. But in carcinoma of the gall-bladder he states almost the reverse, that is, the gall-bladder is palpable in 80 per cent. of the cases and not palpable in 20 per cent.

This law of Courvoisier is generally stated in too sweeping a manner; for example, I have heard very experienced surgeons say that a palpable gall-bladder with the history of cholelithiasis, etc., indicates cancer. But according to the above figures, this is not an absolute rule, as 20 per cent. of cancer of the gall-bladder cases present no palpable gall-bladder. J. C. HEMMETER.]

It is still rarer that the actual observance of a passed stone in the stool permits the diagnosis in the absence of any preceding symptoms. I should, however, emphasize the following syndrome: *If a person who has had an infectious colitis, or dysentery, or typhoid fever frequently complains of gastralgia two hours or three hours after meals, the clinician should exhaust his diagnostic resourcefulness to ascertain the existence or non-existence of gall-stone.*

Case of intermittent spasm of the stomach as reflex neurosis with gall-stones in a man of 38 who had no suspicion of his tendency to cholelithiasis, his recurring gastric spasms having long been supposed to be primary neurosis. The attacks began with severe oppression and pain in the gastric region and the stomach was seen to be distended with gas, but the pulse was regular and not faster than usual and there was no tendency to labored breathing. The attacks sometimes lasted for hours, but there was never any vomiting. The motor functioning was also much exaggerated during the attack.

The development of jaundice finally led to examination of the stools, when it was found that gall-stones could be discovered in the stool sooner or later after each of the spasmodic attacks. After passing 238 gall-stones his patient seemed to be permanently relieved and has been free from jaundice and from all gastric disturbances to date. Buettner (Archiv f. Verdauungskrank. Bd. xvi, Nu. 2, 1910).

Calculi may be present in hepatic or common bile ducts, without clinical or palpatory evidence. Following the suggestions of Kehr, the writer has, in the past 4 years, explored these ducts in 36 cases in which palpation was negative. In 12 calculi were found. Two of these had been operated upon previously by other surgeons. Of the 4 indications given by Kehr, 3 have seemed to the writer of special importance in the order named: (1) the presence of many small calculi in the gall-bladder or cystic duct; (2) an enlarged, thick-walled common duct; (3) the presence of chills, fever, or icterus. To these he adds a fourth, recurrence of pain or symptoms of cholangitis (chills, fever, etc.) after operations, such as drainage or removal of the gall-bladder, or even after either of these combined with choledochostomy. D. N. Eisendrath (Med. and Surg., i, 507, 1917).

Characteristic disturbances occur only, then, when a stone has left the gall-bladder and entered the ducts, or after the presence of gall-stones has led to infections and inflammations of the duct. This condition gives rise to the so-called gall-stone colic. Thereby the stone may be evacuated into the intestine, and eventually pass out of the body; but rarely do all the stones pass out in this manner. For the purpose of diagnosis and treatment it is practical to distinguish the condition of the patient during the attack of gall-stone colic, and, secondly, an irregular course of the cholelithiasis.

The direct and immediate cause of the colic is but little understood. It has been supposed that the stones already existing in the gall-bladder may be forced into the duct by concussions of jolting of the body, by a fall, by strong compression of the abdominal muscles, by vomiting, by operations on the other abdominal organs, by the act of labor, by cold, and by dietetic errors. The typical attack is generally preceded by discomfort, nausea, and a slight chill; but the pain may also start without any premonition whatever and continue in aggravated paroxysms until it becomes intolerable. But even in the intervals a dull, boring soreness is always complained of in the center of the liver. From here the pain may radiate to the right shoulder, epigastrium, spine, and into the legs.

Unusually sensitive patients may become unconscious or pass into a convulsion or delirium; vomiting is a frequent accompaniment. In about one-half of these cases there is a pronounced chill followed by an elevation of the body temperature, which has been called the "reflex fever," but which is more correctly to be interpreted as the index of an infection of the biliary passages.

Enlargements of the gall-bladder only occur in one-third of the cases, and are a consequence of the cholecystitis. Jaundice is an important indication for the interpretation of this colic, but in my experience it was absent in 55 per cent. of all cases of genuine gall-stone colic. The icterus may be observable in the conjunctivæ after twelve hours, and bile-pigments may be present in the urine. There may be icterus without mechanical obstruction of the common gall-duct; this is an inflammatory stagnation caused by the invasion of the bile passages by bacteria; but there may

also be icterus brought about by functional disturbances in the liver-cells due to general infection originating from the gall-duct. The duration of this jaundice is very variable; it rarely exceeds the regular attack of colic more than several days.

In 9 per cent. of 1000 cases studied by the writer, the disease was malignant; in 434 cases there was cholecystitis without gall-stones. A common lesion associated with gall-bladder disease was appendicitis. When stones occurred they did so at any stage of the infective process, large stones forming in as short a time as three weeks. Less than 8 per cent. of the patients were of obese type; 463 had lost considerable weight; 4 per cent. had chronic diarrhea, though most of them had good appetites. There was jaundice in only 161 cases where gall-stones were demonstrated later, and jaundice was observed in 25 per cent. in which there were no gall-stones. F. Smithies (*Trans. Amer. Med. Assoc.; N. Y. Med. Jour.*, June 9, 1917).

Even in intense icterus the stools are not always free from bile. If the feces are sifted through a stool sieve it is sometimes possible to find the stone; but this is not the rule. It is possible that a stone has actually passed, and that it has become disintegrated in the intestinal canal. During an attack of colic it would be an error to assume that a stone has always passed the common gall-duct or the cystic duct, for the pain may be caused by the acute cholecystitis, or the stone may have dropped back into the gall-bladder. The use of the stool sieve will be referred to later on.

After a typical attack of colic they cease after several hours, as a rule, sometimes, however, only to be resumed with renewed severity; thus an attack may be protracted for several days. If

a stone has actually passed, the cessation of pain is abrupt. The pains may be very slight in other cases, or entirely absent in still others, and the passages of a stone only evidenced by transient swelling and sensitiveness of the liver to pressure, or by a very slight icterus. The intensity of the pain is by no means proportionate to the size of the stone, for the irritability and smoothness of the biliary passages, the hardness, shape, and configuration of the stone determine the pain.

There are three distinct areas in which pain exists or in which tenderness may be elicited in cholelithiasis or its complications, namely, the hepatic edge of the gall-bladder region, the subcostal part of the liver, and the dorsal surface. The hepatic free border may be painful *in toto* or more particularly in the neighborhood of the gall-bladder, or the latter alone may be tender. In the great majority of acute cases of cholelithiasis the entire edge is painful to touch, while in the free intervals the pain is more localized at its point of origin. It is also in the acute attack that the subcostal surface is most often found sensitive, sometimes in its entirety, sometimes only in its lower portions. Finally, the dorsal area may be found tender at the level of the two lower dorsal and the upper lumbar vertebræ from 2 cm. to the right of the vertebral column to within the posterior axillary line. Careful palpation must be practised, and when the tenderness is equally marked on both sides or higher up or lower down no diagnostic value should be attached to it so far as gall-stones are concerned. The importance of the dorsal tenderness lies in the fact that it is often present long after the acute attack, and in latent cases or in cases without icterus, in which the diagnosis otherwise would be difficult. An excellent method to test the degree of tenderness of the various areas is by

means of electrodes. In conclusion, the author mentions various conditions which frequently resemble gall-stone colic; these are ulcer of the duodenum, enteroptosis with displaced right kidney, hyperchlorhydria, and intestinal neurosis. S. Boas (Münch. med. Woch., April 15, 1902).

Sharp pain by sudden pressure into a point midway between the umbilicus and the ninth costal cartilage was found by the writer unfailing as a diagnostic symptom of cholelithiasis, and he has verified it repeatedly at operation. When this sign disappears in a patient long under observation, the writer holds that the gall-bladder has emptied itself. Robert Abrahams (N. Y. Med. Jour., Jan. 8, 1910).

The writer found a tender point in the interspaces in 63 per cent. of 73 patients with cholelithiasis. He found Abraham's sign (pain on pressure of a point midway between the umbilicus and the cartilage of the ninth rib) only in 32. The intercostal neuralgia with gall-stones occurs in the ninth, tenth, and eleventh right interspaces, but the most striking sign is a sharp pain felt on pressure of the anterior end of the eleventh rib. These pains and tenderness, generally elicited only by pressure, seem to be characteristic only of cholelithiasis. They are frequently the first signs of a tendency to gall-stones and may prove the forerunners of an acute attack. M. E. Binet (Archives des mal. de l'app. digestif, March, 1911).

In the course of radiographic studies of gall-bladder disease the writer happened to observe in 2 patients total spasm of the stomach, apparently as a reflex from the painful condition of the other organ. Schlesinger (Berl. klin. Woch., June 24 and July 1, 1912).

One should look for tender spots to the right at the level of the gall-bladder, and compare the right with the left side. If there is marked tenderness in the continuation of the



right axillary line, scapular line, the posterior median line at level of gall-bladder, one can be sure of gall-bladder pathology and can safely hand the patient over to the surgeon. Tender spots are present in only one other condition, intercostal neuralgia; they are not present in primary or secondary carcinomas of the liver or when the liver enlargement is due to pancreatic pathology, or in engorged liver due to cardiac decompensation. Friedman (Med. Rec., May 29, 1920).

It is a singular thing that the largest stones may sometimes pass with little pain or no pain at all, namely, by formation of a fistula (see below). I possess a gall-stone which was vomited by one of my patients who rarely complained of abdominal distress. The stone is about as large as a pigeon's egg. It was passed six years ago, and there have been no symptoms since. In rare cases death may result by heart feebleness, collapse or shock, or reflex convulsions during an attack of colic. The number and frequency of the attacks are very variable. It is very rare that a patient has but one attack, for the passage of one stone renders the others movable, and thus we may have groups of attacks that may be repeated at longer or shorter intervals, and may also remain away for several years. In the majority of the cases the progress of a regular attack of colic is a favorable one; but at any time this regular form may pass into the *irregular*.

The irregular manners of progression may be classified under four headings:—

1. Permanent arrest of the flow of bile.

2. Infectious inflammations of the biliary passages (cholangeitis, cholecystitis, abscess of the liver).

3. Ulcerations of the biliary passages, perforation, pericholecystitis.

4. Impermeability of obstruction of the gastrointestinal canal.

It is evident from a survey of these headings that the irregular courses of cholelithiasis represent or lead to surgical conditions almost exclusively, and accordingly the reader is referred to another part of this work, where they are considered from the standpoint of the surgeon.

1. Permanent obstruction to the flow of bile is caused by incarceration of a stone in the ductus choledochus or hepaticus. It is rare that a compression of the common gall-duct is caused by a stone that is wedged in the cystic duct; but strictures and neoplasms that have been caused by gall-stones may also produce the obstruction.

The consequence is a chronic icterus, lasting a very long time, but which is recovered from generally by the passage of a stone through a fistula between the common gall-duct and the duodenum; but sometimes a grave icterus may lead to death. In uncomplicated incarcerations of stone this fatal result is fortunately rare. The evil consequences of a so-called fatal chronic icterus caused by gall-stones are more often due to a carcinoma of the biliary passages. I feel it my duty to emphasize the alarming frequency with which protracted cholelithiasis that is not operated upon later on becomes complicated by carcinoma. This is one of the principal reasons why prolonged, purely medical, or clinical, treatment by non-operative methods is positively unjustifiable, yes, even criminal.

The conditions mentioned under sections 2 and 3 are described in the surgical sections of this work. I must add that perforation may occur from the gall-bladder outward through the ab-

dominal wall and lead to spontaneous cures. More frequent than this form of perforation are the fistulae between the bile passages and the intestinal canal. Those between the common gall-duct and the duodenum are the most important. They occur in the neighborhood of the papilla of Vater and resemble the passage of a stone as if it had occurred *per vias naturales*. Perforations into the colon may occur, but those into the stomach and small intestines, into the retroperitoneal tissues, into the portal vein, into the pleura, lungs, or urinary passages, and into the vagina are very rare. Perforations into the peritoneum are most dangerous.

In reporting a case of ileus caused by gall-stones, the writer recalls that this complication was first described by Bartholin in 1654. In 1914, Wagner collected 334 cases from the literature. Of these, 161 were operated upon. The mortality was 62 per cent. Of the 173 patients not operated on, 93 recovered after spontaneous passage of the stone and 80 died. Since Wagner's publication about 30 cases have been reported. Most of the patients were women and the condition was not preceded by signs of gall-stones. The statistics as to the relative frequency of this form of intestinal occlusion vary from 1 in 15 to 1 in 28. In his own case, the woman, aged 64 years, had for 5 months had pain in the epigastrium and slight fever. There had been no icterus or vomiting and no blood in the stools. A few days before the patient's admission to the hospital the pain had become very intense, the abdomen became distended, and it was impossible to cause a movement of the bowels, even by giving purgatives. An artificial anus was made, but death followed. Autopsy showed dilatation of the first part of the small intestine, the lower third being small and collapsed. There was an opening between the gall-bladder and the

second portion of the duodenum to which the gall-bladder was adherent. At the juncture of the middle and lower thirds of the ileum were two gall-stones. The lower and larger one occluded the lumen.

The diagnosis of ileus caused by gall-stones is difficult during life. As a rule stones pass through an opening between the gall-bladder and duodenum, but sometimes they cause such a dilatation of the common and cystic ducts that they are able to pass through the ducts. If the surgeon finds the intestine occluded by a gall-stone he should always make an examination for other stones which might cause obstruction and necessitate operation later. (Pan-sera, Policlinico, xxviii, 475, 1921.)

4. Impermeability of the gastrointestinal canal. It has been observed that dilatation of the stomach was caused by compression of the pylorus by a gall-bladder filled with stones, but this is fortunately rare. More frequent is the obturation ileus caused by obstruction of the intestinal lumen through large stones that have gotten into the intestine through a fistula.

Analysis of 129 cases in which the writer found pathological conditions in the pancreas in the course of 520 laparotomies for assumed gall-stones and chronic jaundice. In 21 cases the pancreas was the seat of a carcinoma, in 1 of cyst, in 5 of necrosis, and in 102 there was chronic pancreatitis. The pancreas was thus found diseased in 24 per cent. of his 520 gall-stone cases in the last five years. Examination later gave negative findings to the Cammidge test in the milder cases, showing that the drainage of the hepatic duct or removal of the gall-bladder had been followed by the cure of the pancreatitis. The Cammidge test in 40 cases both before and after the operation was positive in 82 per cent. of the cases of chronic pancreatitis. Kehr (Mitt. a. d. Grenzgebieten der Med. u. Chir., Bd. xx, No. 1, 1909).

In a number of cases of gall-stone disease the writer had heard a mitral systolic murmur during and shortly after an attack of colic. It probably depended on temporary dilatation of the heart. The degeneration predisposed the heart to dilatation when, during the attack of colic, the blood-pressure rose. The murmur was loud and unmistakable. The heart was enlarged, but not to any great degree. David Riesman (*Med. Record*, June 3, 1911).

**DIAGNOSIS.**—The diagnosis is not difficult in typical attacks of colic. It is important accurately to map out the exact localization of the pain. Confusion with intestinal, lead, renal, and gastric colic, as well as cardialgia, may readily occur. Icterus is important for the diagnosis, but, as I have said, it was absent in 55 per cent. of my cases. When very slight attacks of icterus are associated with frequently repeated and painful swelling of the liver, this is very important for the diagnosis. The safest conclusion can, of course, be derived from a demonstration of the stones in the passages.

A large number of apparently incorrect diagnoses of gall-stone is recorded in which all classical symptoms seem to be present, and yet, on opening the gall-bladder, no gall-stones are found. An abnormal condition of the gall-bladder inviting infection, causing colic, and in the writer's belief making the gall-bladder the nidus of future gall-stones is the condition present. The only error in such cases is in limiting the cause of symptoms to an actual crystalline formation. On the other hand, the absence of gall-stone pain and discomfort in the patient's history must not be given too much weight in eliminating gall-stones from the diagnosis. Richardson (*Boston Med. and Surg. Jour.*, May 30, 1907).

The diagnosis is too often delayed. In most cases the condition begins before the fortieth year. Almost every

patient will give a history of long-standing dyspepsia, capricious appetite, constipation, flatulence largely independent of meals, and discomfort when the stomach is empty. Later, acute attacks of pain in the right upper abdomen may appear, and finally true biliary colic, with vomiting. A sensation of chilliness is characteristic. Jaundice, hematemesis, etc., as well as laboratory methods, are practically valueless for purposes of early diagnosis from gastric and duodenal ulcer. Deaver (*Jour. Amer. Med. Assoc.*, Jan. 29, 1910).

Cholelithiasis is oftener mistaken for primary digestive diseases by the general physician than is the case with any other organic disease. As in peptic ulcer it is usually hemorrhage that is wanting, so in gall-stone disease it is usually jaundice. This has been observed in less than 5 per cent. of the cases. Gall-stones are found in 7 per cent. of all autopsies, while in autopsies of persons over 60 years of age they are encountered in 25 per cent. The symptoms of cholelithiasis are mainly those of indigestion. Colic is the most prominent symptom. Pain frequently and tenderness of the liver almost always follow the colic. There is a tender area on the right side behind, on a level with the twelfth dorsal vertebra, and extending at times to the posterior axillary line. This is a sign of great value. Jaundice when present usually occurs only after one to several days from the beginning of the colic. R. F. Chase (*Boston Med. and Surg. Jour.*, Oct. 27, 1910).

In gall-stones in the early stages there is a mild gastric disorder with irregular attacks of indigestion coming on suddenly, with gas formation and feeling of epigastric constriction or tightness, chilliness, belching, regurgitation, and vomiting. In the second stage there may be dull or severe pain under the right costal arch, which may be aggravated by food, sudden exertion, or deep inspiration. These attacks are fre-

quently evanescent in type and followed by periods of good health. Unless careful chest examination is made there may be a diagnosis of pleurisy. In making a diagnosis of gall-stone disease the etiological possibilities should be investigated. It is known that it often follows typhoid and pregnancy, and probably any infectious disease that produces toxins. C. C. Coleman (*Jour. Amer. Med. Assoc.*, March 25, 1911).

Attacks of "colic" resembling those due to gall-stones may be the result of movable kidney or of duodenal ulcer. It may be impossible to make a certain diagnosis without operation. In the majority of patients with gall-stones "indigestion" is present for several years before the first attack of colic. This indigestion has certain features which often enable a diagnosis to be made, but is sometimes suggestive of gastric or duodenal ulcer. Sherren (*Lancet*, April 1, 1911).

A certain method of procedure for differentiating gall-stone disease by exclusion is as follows: The examiner first seeks to exclude epigastric hernia, the symptoms from which may simulate those from gall-stones; then he excludes circumscribed peritonitis, gastric ulcer, and cancer. With the former the pains are connected with the meals, while in cholelithiasis the attacks of pain may occur at any time, often suddenly in the night. Duodenal ulcer and affections of the small and then of the large intestine are next considered. Especially with nervous and membranous colitis, the pains are liable to resemble those with gall-stones except that they recur more frequently, and are not accompanied by jaundice. Appendicitis may induce adhesions causing disturbances similar to those from gall-stones. With acute pancreatitis the collapse is severer than with gall-stone colic and the stomach region generally protrudes, while otherwise the trouble may suggest ileus. The possibility of gastric crises should also be borne in mind and

the reflexes tested and hyperesthetic zones sought for. The writer has had cases of coincident gastric crises and gall-stones. Calculi in the kidney may be excluded by roentgenoscopy, and wandering kidney by manual examination. With pain from spastic conditions in the stomach or intestine, the gall-bladder is not specially tender. Differentiation of cholelithiasis is unusually difficult when the patient is inclined to hysteria. Tenderness on palpation of the right hypochondrium and especially at the point where the ninth intercostal nerve pierces the rectus muscle is the most reliable sign of gall-stone trouble when connected with colics. Another characteristic sign is the radiation of the pain to the right shoulder and into the right arm. In some cases this radiated pain dominates the clinical picture, and the patients are treated for years for assumed neuritis until passage of a gall-stone cures the "neuritis." When "neuralgia" of this character is complained of, the skin of the upper abdomen should be tested for extrasensitiveness to contact. The right upper abdominal wall is also liable to be left rigid during and after gall-stone colic. The writer insists on bed rest, possibly for weeks, for patients with gall-stone pains until the region is no longer tender. Hot compresses to the upper abdomen and hot water internally aid in the cure, supplemented by plenty of water to drink and five meals a day of readily digestible food to keep the bile flowing freely. The meal is the best cholagogue, he adds, and no pharmaceutical means are known to dissolve or expel gall-stones. F. Schultze (*Jour. Amer. Med. Assoc.*, from *Med. Klinik*, Oct. 1, 1911).

Only in exceptional cases is it possible to state positively the presence of gall-stones. Even with the writer's 1668 gall-stone operations he still makes mistakes in diagnosis of cancer of the gall-bladder, especially when it is associated with empyema. With chronic empyema the tempera-

ture may be persistently within normal range in 50 per cent. of the cases. The history is of peculiar importance for the diagnosis of chronic empyema of the gall-bladder and chronic obstruction of the common bile-duct, and he makes a point of writing it out and reading it over carefully two or three times to weigh it in all its bearings. A diagnosis based on the history is liable to be more correct than one based on the actual findings at the moment. H. Kehr (Münch. med. Woch., March 21, 1911).

In chronic cholelithiasis the pain may be confined to the epigastrium and differ in no respect as far as location goes from the pain of gastric ulcer or nervous gastralgia. The jaundice, too, which is regarded as a cardinal symptom, is often absent. On account of the ease with which a gastroptosis and a prolapsed right kidney can be found in women on account of their lax abdominal walls one is often wont to ascribe their attacks of pain in the upper abdomen to this cause; nothing could be more unjustifiable unless a careful investigation of the gall-bladder region is made. A prolapsed right kidney may not only simulate gall-stone disease, and *vice versa*, but may actually be one of the exciting causes of such formation. Conversely a purulent gall-bladder may simulate a pyonephrosis. A. E. Austin (Boston Med. and Surg. Jour., March 28, 1912).

Five cases which confirm the value of the method of diagnosis of cholelithiasis by microscopic examination of the sediment of the stomach content siphoned out three-quarters of an hour after ingestion, fasting, of 150 or 200 c.c. (5 to 6¾ ounces) of olive oil. The findings are rendered much more reliable, however, if the passage of bile into the duodenum and its reflux thence into the stomach are promoted by massage of the liver and gall-bladder region and by the addition of a little glycerin to the oil, and by administration of atropine. Demattheis (Gaz. degli Ospedali, Feb. 25, 1912).

The X- or Roentgen rays are of no utility in the demonstration of gall-stones. I have personally placed eight large gall-stones in a row one behind the other and obtained no impression on the plate by Roentgen photography.

Of 93,000 patients examined, stones were noted in only 133, making 0.14 per cent., while, on the other hand, at autopsies fully 10 per cent. of the bodies are found to possess them if a careful examination of the biliary system is made. The great frequency with which gall-stones are not diagnosed *intra vitam* is thus shown. The Roentgen rays may be looked upon as a valuable diagnostic aid in the future, and already a number of excellent photograms have been published. Best results will always be obtained with the strongly calcareous stones, while the rarer ones consisting chiefly of cholesterolin or bile-pigment can hardly be expected to throw a shadow. H. Fiedler (Münch. med. Woch., Oct. 22, 1901).

Case in which the symptoms indicated kidney-stone and radioscopy showed a large concrement in the right side. Its shadow was 40 mm. in diameter when the tube was placed above the patient, but the shadow was only 28 mm. in diameter when the tube was placed beneath, the patient's position and the distance of the tube being similar at each exposure. This difference in the size of the diameter with the upward and downward exposures indicated that the stone must have been much nearer the front than the back of the body, suggesting that it was in the gall-bladder rather than in the kidney, although there had been no signs of anything wrong with the biliary apparatus. Bécclère (Bull. de l'Acad. de Méd., June 28, 1910).

If adhesions in the gall-bladder region have taken place we have in the Roentgen rays a means of diagnosis which is distinctly more valuable than the direct examination for gall-stones. Recognition of the effects of these adhesions will explain the indefinite symptoms occurring in

these cases. The anatomical conditions must be understood. The normal stomach is situated on the left side of the abdomen, seldom extending more than an inch beyond the median line when in the standing posture. The pylorus is located about an inch above the umbilicus, and the lower pole in the normal stomach is about on a level with the lower pole of the pylorus, but in the average adult it is distinctly lower and may be as low as the crest of the pubes in gastropotosis. In chronic cholelithiasis and cholecystitis the swelling of the liver and gall-bladder causes them to approach the duodenum and stomach and conduces to adhesions between the organs. When the swelling goes down they pull the duodenum and stomach upward and to the right, and the clinical symptoms appear during the period of digestion when the motor function of the stomach is at its height, and especially when the adhesions interfere with the emptying of the gall-bladder, causing a dragging after a large meal. During active peristalsis these adhesions are pulled on, and if there is an inflammation an aching pain is felt. In such cases the writer examines the gall-bladder area to detect if possible the presence of stones, and he gives the usual bismuth mixture (bismuth subcarbonate, 1 ounce to a glass of buttermilk), and observes it carefully by the fluoroscope, the patient standing. Instead of dropping quickly to the lower pole, as it does normally, it is carried more slowly to the right of the median line and directly above the umbilicus. The influence of pressure on the stomach must also be studied. He also believes that taking a plate is equally important, and makes one or more after the fluoroscopic work. The adhesions of course influence the position of the stomach and duodenum. Sometimes the latter alone may be chiefly affected. Conclusions as to the position are of no value unless they are based on a full knowledge of the normal position of the stomach and the

conditions which influence it, such as pressure, varying degrees of fullness, etc. The effects of adhesions on the peristaltic waves should also be observed by the fluoroscope. Adhesions due to carcinoma can sometimes be recognized by the encroachment on the stomach lumen, but the general history and other evidence and even an exploratory operation may be necessary. G. E. Pfahler (*Amer. Jour. of Surg.*, from *Jour. Amer. Med. Assoc.*, June 17, 1911).

The diagnosis of gall-stone disease can positively be made only after an attack of colic or the stone be expelled through the intestinal tract. All other symptoms, such as jaundice, seat of pain, frequent repetition of same, the presence of gall-bladder tumor, etc., are of doubtful nature. These symptoms may lead to errors in diagnosis, such as diseases of the stomach, of the intestines, of the pancreas, of the kidney, and even of disease of the central system, all of which can produce similar symptoms.

The most difficult is the differential diagnosis of diseases of the stomach, of the duodenum, and of the pancreas. The pain in gall-stone colic is not seldom in the region of the epigastrium, *i.e.*, in the middle line, instead of on the right side. This is particularly true in cases of pericholecystitis with adhesions to the stomach or duodenum. The Roentgen examination hitherto has not given us trustworthy results, except in cases of stones containing lime salts. C. A. Ewald (*Amer. Jour. of Gastroenterology*, Oct., 1912).

A résumé of the recent literature shows that the consensus of opinion at present is that in at least 50 per cent. of the cases of gall-stone condition, the stones can be diagnosed by the X-ray. F. W. O'Brien (*Boston Med. and Surg. Jour.*, Mar. 2, 1916).

The writer urges the importance of differentiating between right renal lithiasis and gall-bladder lithiasis, noting the embarrassing position in which the surgeon is placed through having accepted an incomplete and

erroneous finding by the röntgenologist. Approximately 20 per cent. of gall-stones are of sufficient density to cast a shadow in a right kidney plate, and 5 to 6 per cent. contain calcium deposits in a sufficiently extensive and uniform degree to render differential diagnosis difficult. The physical characteristics of the two conditions are as follows: *Renal calculus*, very dense; usually single; of uniform density; if multiple, irregular in shape conforming to the pelvis and calices; if multiple, varying in size and shape; with surface usually rounded; frequently branching; seldom changing in position between examinations. *Biliary calculus*, soft or dense; usually multiple; of variable density; if multiple, conforming to the shape of the dilated gall-bladder; if multiple, relatively the same in size and shape; with surface usually flat or faceted; never branching; frequently changing in position between examinations. L. G. Cole (Interst. Med. Jour., xxiv, 946, 1917).

The X-rays may be useful, however, when it becomes necessary to differentiate gastric ulcer or gastric carcinoma from gall-stone disease, for, according to my method described in the Archiv f. Verdauungskrankheiten, Berlin, 1906, ulcers and cancers of the stomach can be made visible and demonstrated by this form of photography.

[That the application of X-ray photography for the diagnosis of ulcer and cancer of the stomach was original with me is now acknowledged by Holzknecht and Handek, of Vienna, and by Mathes, of Cologne. The article just quoted is the first one published by anyone on this subject. (See also "Bedeutung d. Magenradiologie," etc., by Paul Clairmont and Martin Handek, Vienna, 1911.) J. C. HEMMETER.]

For the diagnosis of the irregular forms, the previous history of former attacks is of great importance.

**ETIOLOGY AND PATHOGENESIS.**—The principal factor in the

formation of gall-stones is a catarrh of the biliary ducts and gall-bladder, which is traceable in the majority of cases to an infection of the gall-bladder by micro-organisms. Stagnations in the flow of bile favor the development of this catarrh; but there is a second factor which leads to the formation of gall-stones, to which little reference is made, and to which the writer first called attention. It consists mainly of pathological alterations in the chemical composition of the bile. At the bottom of all this is an abnormal intermediate metabolism of the liver. To this view we are inclined because at many operations for gall-stone the gall-bladder itself, as well as the stone, the bile, and the various gall-ducts, was found to be free from bacteria; all cultures were negative.

Naturally it has been asserted that there may be bacteria which require such a culture medium as cannot be imitated outside of the living tissues of the body, and that these may cause gall-stone or inflammation of the biliary apparatus. This is a very far fetched hypothesis, for there is no doubt that the only bacteria which are here concerned are those which originate from the intestine, and for all the more important intestinal bacteria there has been no difficulty of finding adequate culture media.

The writer has attempted to ascertain three points: Whether bacteria were to be found in the normal gall-bladder; whence come those found in the diseased gall-bladder; what are the factors co-operating in the disease and which are the most important bacteria concerned. The study was based on the literature of the subject and his own clinical and experimental researches. In 6 personal cases the conditions indicated in all

that a cancer had developed first and had been followed by gall-stone production. The symptoms from the gall-stones were the first sign of trouble in some. In a previous series of 7 cases conditions indicated infection from the intestines or from the blood and liver or both as an important factor; secondary muscular insufficiency was another frequent factor. The combination in the gall-bladder of typhoid and colon bacilli or tubercle bacilli, and of typhoid and cancer is not infrequent. Baron (*Beiträge z. klin. Chir.*, Feb., 1912).

In speaking of the direct etiology we must consider everything which could produce stagnation of the bile-flow. Among these we must consider compressing clothing, insufficient bodily exercise, dislocation or compression of the bile-ducts by tumors, cicatrices. Among the causes which are little recognized I wish to call attention to one of which I have convinced myself repeatedly at autopsies, that is, enteroptosis, and gastropoptosis especially. The displacement of the stomach may cause traction upon the hepatoduodenal ligament. This I have frequently seen at abdominal sections undertaken for gall-stone. Another cause is dislocated or floating kidney. Then, there seems to me to be a form of atony of the musculature of the gall-bladder, which in some way is dependent upon the traction caused by dislocated abdominal viscera in enteroptosis. The tugging upon the splanchnic and abdominal branches of the vagus interferes with the reciprocal innervation that exists between the sphincter at the papilla of Vater and the musculature of the gall-bladder. A close relationship seems also to exist between gall-stone disease and pancreatitis.

When anatomical conditions are favorable, disease of the pancreas may occur as a complication of chole-

lithiasis when a calculus passes along the common bile-duct. The lodgment of a stone near the orifice of the bile-duct, where it may at the same time compress and occlude the duct of Wirsung, is not uncommonly a cause of pancreatic lesions and disseminated fat necrosis. Should a calculus become impacted in this position, one of several conditions may result:—

1. An individual, usually in fairly good health, with perhaps a history of previous gall-stone colic, is suddenly attacked with pain in the epigastric region, accompanied by vomiting and followed by collapse. Death follows usually within forty-eight hours, and at autopsy gall-stones are found in the bile passages, while that one which caused the fatal attack may be still lodged in the common duct near its orifice. The pancreas is enlarged, infiltrated with blood, and hemorrhage may have occurred into the surrounding tissue. Foci of fat necrosis are usually present.

2. A fatal termination may not follow rapidly the symptoms mentioned. Pain in the epigastrium persists, jaundice may be present, and a tumor mass above the umbilicus may indicate a probable lesion of the pancreas. At the end of one or more weeks or months death occurs, often with symptoms indicating the presence of suppurative inflammation, presumably in the neighborhood of the gland. At autopsy the diagnosis of cholelithiasis is confirmed by the presence of gall-stones in the gall-bladder or in the bile-duct, and occasionally the offending calculus is still lodged near the junction of the common bile-duct and the duct of Wirsung. The pancreas is dry, black, and necrotic, and evidence of previous hemorrhage may be present. Secondary infection has occurred and the pancreas lies in an abscess cavity formed by the bursa omentalis. In the wall, and often widely disseminated in the abdominal fat, are foci of necrosis. Since the individual has survived the primary lesion opportunity has been given



for the development of secondary changes in the injured pancreas and neighboring fat.

3. In certain instances long-continued or repeated obstruction of the pancreatic duct by gall-stones does not cause the acute lesions described, but produces chronic inflammatory changes. E. L. Opie (*Amer. Jour. Med. Sci.*, Jan., 1901).

In December, 1907, the writer, in reviewing his operative experience in the surgery of the upper abdomen, found that in 2200 operations on the gall-bladder and biliary passages the pancreas was coincidentally involved 141 times, 6.1 per cent. As the total of all pancreatic diseases operated on was only 168, the fact was developed that 81 per cent. were due to or accompanied by gall-stones. The writer describes the anatomical conditions and the development of the pancreas, showing that in 62 per cent. of human subjects the terminal third of the common bile-duct is imbedded in pancreatic tissue; hence, in that proportion of cases structural change in that portion of the pancreas will interfere with the liver excretion, while a stone in the terminal portion of the common duct, or infection caused by stone in any part of the bile tract, exposes the duct of Wirsung, and through it the pancreas, to infection. In this unfortunate association of terminal facilities the larger percentage of known diseases of the pancreas have their etiology (Opie). The "triangle of pancreatic inflammation" is that part of the head of the pancreas which lies between the duodenum on the right and the ducts of Santorini and of Wirsung below. There is evidence that catarrhal jaundice, especially the epidemic form, is probably due to pancreatic disturbance, and is similar to like inflammation of the parotid gland in mumps. Acute pancreatitis is mentioned; its most interesting feature is fat necrosis, which the writer thinks is probably the result of pancreatic juice which has become activated by associated ferments, either from the

bile or the duodenal mucosa, rather than to the normal secretion. In resections of the stomach the writer has lacerated the surface of the pancreas many times, but never saw fat necrosis follow. He thinks that there is an exaggerated notion as to its fatality; our knowledge of the condition has heretofore come largely from the morgue; hence, the condition has seemed a very fatal one. The greatest interest in connection with gall-stone disease concerns the chronic forms of interstitial pancreatitis, of which mild infection and interference with drainage appear to be the main etiological factors. There are two forms, the interlobular and the inter-acinar, the former being fortunately, the most commonly associated with gall-stone disease. In the inter-acinar form the pancreas feels smooth and tough, instead of rough and nodular, as in the other form, and is apt to be associated with glycosuria, owing to the involvement of the islands of Langerhans. The interlobular type, however, may progress sometimes till these are involved and a secondary diabetes occurs. Chronic interstitial pancreatitis may last for years without symptoms to differentiate it from the original disease, but if its possibility is borne in mind and careful search reveals pancreatic changes an early resort to surgery is indicated. Jaundice is one of the chief symptoms and may last for years. The emaciation is extreme and the pigmentation more marked than with the ordinary uncomplicated common duct-stones. A history of gall-stones can usually be obtained, and in thin patients the enlarged pancreas can sometimes be felt as a hard mass across the upper abdomen. Careful examination of the stools should be made; large, light-colored, greasy stools, without jaundice, are indicative of pancreatitis. Cammidge's crystals in the urine are also mentioned as of probable diagnostic value. The writer has not found that chronic pancreatitis greatly influences the prognosis after gall-stone opera-



# Varieties of Gall-stones. (*Walton.*)

**CHOLESTERIN.** 1, pure cholesterin; 2, cholesterin mixed with bile pigment; 3, cholesterin with calcium carbonate and pigment; 4, crystalline cholesterin with outer layer of bilirubin calcium.

**PIGMENT.** 5, pure biliverdin; 6, biliverdin with outer layer of cholesterin; 7, pure bilirubin calcium; 8, bilirubin with outer layer of cholesterin.

**MIXED LAMINATED.** 9, 10, alternate layers of bilirubin and cholesterin; 11, large single non-faceted laminated calculus. This had ulcerated through into the intestine and had caused obstruction.



tions, although there is a much greater tendency to hemorrhage when it exists. The necessity of clearing out all the calculi from the common duct cannot be too strongly emphasized, and they never feel satisfied till assured that none have escaped detection. After clearing out the stones, a large malleable probe should be passed through the common duct to secure good dilatation. Robson has shown that free drainage for the bile is essential and generally suffices for a cure. Cholecystostomy and preferably cholecystenterostomy are the indicated procedures. In the writer's experience removal of stones in the common duct, with temporary external drainage, has given a symptomatic cure. When no stones are found in the common duct or gall-bladder, other things being equal, they prefer cholecystoduodenostomy, and out of 24 cholecystenterostomies 9 were performed for this cause. The writer accounts for the lesser number of cases of pancreatitis with gall-stone disease observed by him than by Robson by his counting only the cases in which the diagnosis was plain. W. J. Mayo (*Jour. Amer. Med. Assoc.*, April 11, 1908).

The greater frequency of these etiological factors in the female sex explains the observation that gall-stones occur 3 to 5 times more frequently in women than in men. They also occur more frequently in old age. Prior to the thirtieth year only 2 to 3 per cent., and after the sixtieth year 25 per cent., of the observed gall-stone cases occur.

In 145 cases of cholecystitis studied by the writer gall-stones occurred in 55.8 to 58 per cent. of patients between the ages of 15 and 45. Adding to these the cases in which symptoms started in that period, the percentage is increased to 65. Gall-stones are not found at autopsy in any larger proportion of cases after 45 than before that age. Ryerson (*Can. Med. Assoc. Jour.*, Sept. 1, 1911).

There has been an enormous increase in the number of cases of cholelithiasis since the beginning of the war. This is due to the increased nervous strain involved. Married women are especially liable to gall-stone disease, and they are now especially subjected to worry. Boas (*Surg., Gynec. and Obstet.*, May, 1916).

Analysis of the gall-stones removed in 14 cases of diagnosed cholelithiasis, showed that in every case where there was a history of previous infection, the gall-stones removed were composed of calcium salts, while in those cases with no history of an infectious disease, the stones were composed of cholesterol. This confirms the previous reports of both Mignat and Rosenow, who have shown that cholesterol stones have no relation to previous infection, while calcium stones usually follow upon a previous or an existing infection. J. Rosenbloom (*Jour. Amer. Med. Assoc.*, lxi, 1765, 1917).

Experience with 240 operative cases of gall-stones showed the preponderance of cholelithiasis in women, and the age between 25 and 30. Fully 89 per cent. of the women had borne children, 13 had had from 13 to 19 pregnancies, and in 36 per cent. the first disturbances had been noticed during a pregnancy. The phenomena observed confirm that hypercholesterolemia is a constant factor in cholelithiasis, in women, at least. Althabe and Nicholson (*Semana Medica*, Buenos Aires, Apr. 11, 1918).

It is of great importance to bear in mind the great rôle which certain infectious diseases play in the causation of cholelithiasis. As a rule, these agents first cause a cholangitis and cholecystitis, and thereafter the injured mucous membranes of these parts produce altered secretions, and possess lessened resistance to the microorganisms that have invaded these parts. One-third of my gall-stone

cases had a previous history of typhoid fever, and I am inclined to look upon this infection as a very serious cause of gall-stones.

The size of the gall-stones varies from that of a sand-grain to that of a hen's egg and even larger. Their number may vary from a single one to a thousand. The form is very manifold; they may be round, oval, pear shaped, mulberry shaped, polygonal. Faceted stones arise by the friction of several concretions which are pressed against each other while they are still in a rather soft state. They may be of any color, white, yellow, gray, green, brown, even black; this color depends upon the external stratum of the stone, and need not necessarily represent the color of the interior. Most gall-stones consist of a hard, stratified shell, containing a soft interior. Generally there is a small, hollow space in the center of this interior if it happens to be a perfectly dry stone.

They are mainly composed of bilirubin calcium, 15 to 30 per cent., and cholesterin, 60 to 80 per cent. There may be also a small amount of calcium carbonate, traces of copper and iron; also remnants of disintegrated epithelia and mucus. The pure cholesterin stones, which are white or yellowish, sometimes even transparent, are rare; the calcium-carbonate stones are very rare. The material for the formation of the stone is furnished by detached and disintegrated epithelia. Several of these features are illustrated in the annexed colored plate.

The direct cause of the stone formation, then, is a catarrhal inflammation of the biliary apparatus, due mainly to micro-organisms, but which, in my opinion, can be due to a pathological

metabolism of the liver. The stones at first consist of soft masses, which become coated with a thin shell. The continued growth is produced by concentric layers of cholesterin and bilirubin calcium on the outside, but at the same time there may be a progressive infiltration of the hollow space in the center with cholesterin.

Cholelithiasis is one of the manifestations of the uric-acid diathesis; it is frequently accompanied by other signs of this uric-acid tendency. There is a certain regularity in the development of the gall-stone troubles; a number of attacks may occur over a period of six to eight weeks and then there may be a pause for several months. The patients frequently connect the attacks with certain seasons. During these periods the slightest error in diet may bring on the colic, while during the intervals gross errors in diet are tolerated without harm. These free intervals explain the benefit frequently ascribed to certain drugs or measures which the patient happened to be taking at the time the free interval arrived. Biernacki (Wiener klin. Woch., April 27, 1911).

The stones are most frequently found in a free state in the gall-bladder; they are very rarely adherent or encapsulated. The gall-bladder is always the seat of a cholecystitis, which is partially the cause and partially the result of the gall-stone. Frequently the walls of the gall-bladder are thickened and contracted; the muscular and mucous layers are atrophic. I have seen the walls of a hyperplastic gall-bladder so tightly contracted around a stone as large as a pigeon's egg that it could only be cut away with considerable difficulty. The gall-bladder is rarely dilated. The bile which is contained in the bladder is abnormally rich in mucus and disintegrating epithelial

**cells.** Stones that occur in the cystic and common gall-duct originate in the gall-bladder, but, once in any duct and lodged there, they can continue to grow in size in the new position. A most frequent seat for the stones to become lodged in the ducts is the diverticulum of Vater, just in front of the orifice of the common gall-duct. Stones which lodge here and close up the orifice may produce a damming back of the bile into the pancreatic duct and eventually lead to inflammation of the pancreas and consequent fat necrosis.

The fact that 86 per cent. of all the Mayos cases of pancreatic disease seen at operation were attended by gall-stones emphasizes very strongly the association of these conditions.

Three mistakes are sometimes made: 1. In the case of acute suppurative cholecystitis, there is a temptation to wait too long before operation. 2. In cases of chronic dyspepsia with upper abdominal pain, the diagnosis may often be made more satisfactorily by exploratory section than by months of indeterminate delay. 3. On the other hand, there is too great a tendency to explore in cases of chronic jaundice, when further observation would make clear a diagnosis of malignant disease. J. E. Jennings (Long Island Med. Jour., Sept., 1912).

The gall-ducts may become enormously dilated in consequence of stagnation in them caused by a stone. It has been observed that small stones, composed of bilirubin calcium, occur in the intrahepatic bile-channels, and this when the gall-bladder and gall-ducts are normal. Evidently these tiny stones are due to faulty metabolism in the liver itself, and this to my mind constitutes one of the important evidences of the theory that there is a form of cholelithiasis which

does not depend upon bacterial infection.

[A thorough insight into the pathological physiology of gall-stones is furnished by Oddi, in the *Monitore Zoölogico Italiano*, Anno V, 1894, "Di una speciale disposizione disintere allos bocco de coledoco." This is translated into German by Winterstein in the German edition of Luziani's "Physiologie des Menschen," II Band, S. 188. Doyon (Arch. de physiol. normale et pathol., 1883-84) also published a beautiful experimental research.

These investigations deal with the reciprocal or contrary innervation between the gall-bladder and the sphincter of the papilla of Vater, a physiological mechanism which is seriously disturbed in splanchnoptosis. This congenital abnormality may thus predispose to cholelithiasis. J. C. HEMMETER.]

The writer found stones in the liver (intrahepatic cholelithiasis) in 6 out of 72 cadavers showing evidences of cholelithiasis from a series of 250 cadavers examined. Intrahepatic concretions apparently require three factors for their production, stagnation of bile, cholangitis, and a tendency to stone formation. That stones lurking in the liver may explain certain cases of supposed re-formation of gall-stones is possible. The stone may induce inflammation in the liver or may pass into the gall-bladder or bile-duct and continue to increase in size. Beer (Archiv f. klin. Chir., Bd. lxxiv, Nu. 1, 1904).

The writer holds that there are cases which are unattended by infection at the time of the attack of colic, and also cases in which an associated high temperature may be due to a complicating disease. He also questions Riedel's statement that dropsy always begins an attack of cholecystitis. Every case of gall-stone colic with rise of temperature demands examination to detect inflammation gangrene and pericystic involvement, or excessive enlargement and possible rupture. Absence of fever indicates a condition which is devoid of danger and warrants delay in surgical procedures. A favor-

able condition also exists when the gall-bladder is neither tender nor enlarged. Pantzer (*Amer. Jour. of Obstet.*, Nov., 1907).

Gall-stones have been found in about one-tenth of all autopsies reported from European and American hospitals. Although this is an extraordinary frequency, it is interesting that the mere presence of gall-stones in the majority of cases causes no symptoms.

The sequence of pathological changes produced by wandering gall-stones is as follows: 1. Development of the stones or stone in the gall-bladder. 2. After-infection of the interior of the gall-bladder. 3. Suppuration and ulceration of the lining of the gall-bladder. 4. Coincident adhesions of the gall-bladder to the transverse colon, to both omenta, and possibly to the duodenum and mesocolon. 5. Perforation of the gall-bladder by extension of the ulceration, with adhesions strong enough to resist the pressure of the escaping contents of the gall-bladder. 6. Encysting fibrous sac. 7. Gradual working downward of the abscess and contents. Estes (*Med. News*, Dec. 23, 1905).

The bacterium which is the cause of the gall-bladder infection cannot always be isolated from the bile, although it may be from the wall of the bladder and the center of the stone. It is not necessary to undertake puncture of the gall-bladder through the intact abdominal wall in order to endeavor to ascertain the specific micro-organism. This can be done by duodenal intubation, often gentle massage of the gall-bladder through the abdominal walls, by setting up of the bile-evacuating mechanism by injecting HCl and albumoses into the duodenum. In case there is an obstruction of the cystic or the common gall-duct, this procedure cannot prove successful. But if any bile reaches the duodenum at all, it can be aspirated by the method of duodenal intubation first practised

by the author in 1897. J. C. Hemmeter (*Med. Rec.*, xciv, 575, 1918).

**PROGNOSIS.**—For those cases which run a regular course, the prognosis is, in general, favorable; but for those cases which run an irregular course, the prognosis is favorable or unfavorable according to the seriousness of the complications.

Owing to the erroneous statement, based on conclusions drawn without warrant from the post-mortem examinations, and so frequently repeated in the literature of cholelithiasis, to the effect that in the great majority of instances gall-stones are unproductive of either symptoms or serious complications, the impression that, as a rule, gall-stones are void of a serious danger has obtained widespread credence. This, together with the fact that the diagnosis of gall-stones seldom has been made prior to the onset of complications, has resulted in gall-stone surgery becoming largely the surgery of terminal events. Occlusion of the cystic duct from inflammation excited by the irritation of gall-stones, as well as the direct blockage of the duct by stone, so frequently rendered permanent by contraction of the inflamed duct about the offending concretion, must be looked on as a terminal event in the progress of cholecystitis, itself a complicating and comparatively late event in gall-stone disease. The still later sequential phenomena of hydrops, empyema, gangrene ulceration, perforation and rupture of the gall-bladder, as well as sclerosis, contraction and obliteration, and malignant disease, are terminal events of a higher degree. From observation and from a study of the literature of the subject, the writer is convinced that the frequency with which rupture of the gall-bladder occurs as a terminal event in gall-stone disease is scarcely appreciated. These cases are commonly diagnosed as peritoneal infection from appendicitis, operated on as such, and so recorded, unless gall-

stones, correcting the diagnosis, are found in the peritoneal cavity. C. N. Smith (*Amer. Jour. of Obstet.*, Jan., 1910).

Is the operation dangerous? The writer ascribes the mortality met with after the operation to two causes: 1, that many patients and many physicians delay seeking the aid of the surgeon until an extensive suppuration exists in the minute biliary passages, or an inoperable carcinoma has developed, when the death of the patient is ascribed to the operation, or to the operator; 2, that the operation is a rare one and is performed by inexperienced operators, whose technique is not perfect. This operation when performed rightly and at the right time is without danger. Kehr (*Munch. med. Woch.*, March 21, 1911).

In 121 cholecystectomies performed since 1912, the writer had 2 deaths, a mortality of 1.6 per cent. In 42 cholecystostomies there were 4 deaths, or about 9 per cent. mortality. Before 1912, gangrenous and suppurating gall-bladders were usually removed; now they are usually drained under local anesthesia. The stage in which the operation is done exerts a great influence on the mortality. In 114 cases of cholecystectomy in the first stage, irrespective of date or technique, the mortality was 0.88 per cent. In 101 operations in the second stage, 67 being ostomies, there were 4 deaths, a mortality of 3.9 per cent.; after 54 operations in the third stage, there were 18 deaths in which the operation or biliary condition was a factor, a mortality of about 32 per cent. Thirty of these patients had acute gangrenous or suppurative cholecystitis, 7 an acute pancreatitis with fat necrosis. W. Wayne Babcock (*Jour. Amer. Med. Assoc.*, Oct. 23, 1915.)

#### TREATMENT. — Prophylaxis. —

The patient must avoid all foods which might possibly lead to indigestion, and thereby predispose to infection of the biliary passages. It is very essential to insist on **small meals**, because a

food which in itself is not harmful may bring on an attack of colic by its bulk. A diet that is rich in fats must be strictly avoided. A diet that gives rise to much gas must be strictly avoided; for instance, peas, beans, lentils, sauerkraut, pies, mayonnaises, salads, and raw fruit. It is essential to avoid alcohol in anything exceeding one-half a pint of light Rhine wine per day. Beer is poisonous for these patients. It is important that the patient should attend to regular evacuation of the bowels, but the strong purgative mineral waters like Hunyadi Janos and Rubinat Condal must be strictly avoided. These powerful mineral purgative waters do more harm than good. Gall-stone sufferers must avoid all clothing that tends to constrict the abdomen.

The course to pursue in aiming at a treatment of cholelithiasis that is based upon the cause would be first to ascertain the specific bacterium which is causing the infection, and thereafter to obtain a serum by inoculating animals with this special strain of organisms. The principle of non-surgical treatment of cholelithiasis is to bring about a period of quiescent latency in the disease. The employment of so-called cholagogues, especially a number that appear to be proprietary articles, is condemned. The use of olive oil, either by mouth or rectum, in large doses, has not been followed by gratifying results. J. C. Hemmeter (*Med. Rec.*, xciv, 575, 1918).

**Treatment During an Attack of Colic.**—The patient must be put to bed immediately; a **hot-water bag** is to be applied over the liver, and  $\frac{1}{4}$  grain of **morphine** is to be injected hypodermically at once. The drinking of small quantities of **hot water** during the attack, or **hot Carlsbad-Sprudel water**, only 2 ounces (60 c.c.) at a



time, is to be recommended. When the patient has recovered from his immediate colic attack I recommend to him to continue the use of the hot Carlsbad-Sprudel water morning and evening, one tumblerful before breakfast as hot as can be taken; then allow one hour to elapse before taking any food. If a slight chronic icterus continues after an attack of colic, and especially if the liver and gall-bladder regions are sensitive, I advise all patients to continue this Carlsbad treatment for a month. In this period the patient must lie down for three hours twice daily, say from 9 to 12 in the morning, and from 3 to 6 in the afternoon, and **hot cataplasms** must be applied to the liver region during this time. During the first hours in the morning he should drink 100 c.c. ( $3\frac{1}{2}$  ounces) of Carlsbad-Sprudel water every fifteen minutes, as hot as can be taken. In this way the patient may drink 600 to 800 c.c. (20 to 27 ounces) in a day. If the patient cannot tolerate so much, the amount of Carlsbad water taken can be restricted, particularly in the afternoon. During this treatment, the meals are taken at 7.30 A.M., 1 and 7 P.M.

**Medicinal Treatment.** — Gall-stones cannot be dissolved by any medicines that can be taken by the mouth. All medicines that have hitherto been supposed to have had this power bring about their only apparent and very transient improvement by their anodyne effect. Thus the **Durand drops**, which are composed of 1 part of turpentine, 4 parts of ether, 20 to 30 Gm. (5 drams to 1 ounce) of cognac, and the yolks of two eggs, act simply as an anodyne. The dose is 15 to 60 drops (0.9 to 3.6 c.c.). Olive oil, oleate of soda,

glycerin, preparations made from bile and bile-salts are of doubtful value.

**Glycerin** (pure and neutral) is effective in the treatment of hepatic colic. Administered by the stomach, it is absorbed by the lymphatic vessels, and notably by those which go to the hilus and the gall-bladder; it can be found in the blood of the sub-hepatic veins. It is a powerful cholagogue, and is a valuable remedy in hepatic colic. A relatively large dose (20 to 30 Gm.— $\frac{3}{4}$  to 1 ounce) of glycerin will frequently bring the crisis to an end. A small dose (5 to 15 Gm.— $\frac{1}{6}$  to  $\frac{1}{2}$  ounce) taken each day in a little alkaline water will prevent further attacks. The small daily dose may be taken for months or years without bad effect. Plautier (*La Tribune méd.*, June 15, 1907).

While in certain cases of gall-stones the knife is the only effective means of cure, in certain other cases a cure occurs without any treatment. Besides these, however, there is a group in which cholelithiasis can be cured by stimulating the secretion of bile, and for this purpose nothing surpasses a mixture of 10 or 15 Gm. ( $2\frac{1}{2}$  to 4 drams) of **medicinal soap** with mucilage of acacia, q. s. to make 60 pills; 3 pills daily after meals. The pills can be supplemented by **enemas of olive oil**. This treatment is to be commenced on subsidence of the acute attack; during this, **belladonna** or **atropine** may be required. This soap treatment was introduced by Senator, and some experiments reported this year from Pawlaw's clinic confirm this cholagogue action of soap. Mosse (*Thérapie der Gegenwart*, Bd. lii, Nu. 12, 1911).

The value of **olive oil** has not proven very great in the writer's hands. It can be useful only for the simultaneous colitis and spastic constipation not infrequently complicating cholelithiasis. Paul Mayer (*Lancet*, June 1, 1912).

I have seen cases in which the **sodium salicylate** seems to act as a very

effective anodyne, and even reduce the jaundice and size of the liver. We do not know in what way salicylate of soda influences the metabolism of the liver-cells, but we do know that it is an intestinal disinfectant to a certain extent, and I have convinced myself that the bactericidal effect of the bile is increased after two days' taking of 60 grains (4 Gm.) of salicylate of soda in divided doses. These tests were made with the colon and typhoid bacilli.

**Sodium salicylate** is of decided value in cholelithiasis. It is given between the attacks in doses of 7 grains (0.45 Gm.) four times daily. Fifteen one-hundredths grain (0.009 Gm.) extract of **belladonna** is usually added. The medication is continued for three or four weeks, **hot applications** being made **over the liver** for two or three hours every morning and evening. It has about the same effect as a course at Carlsbad, providing the salicylate be dissolved in warm Carlsbad water. Chauffard (Berl. klin. Woch., May 8, 1905).

The writer knows nothing better among the medicinal agents used for the treatment of cholelithiasis than the following combination recommended by Billings:—

**R Sodium salicylate.** gr. xv (1 Gm.).  
*Sodium phosphate* ..... gr. xxx (2 Gm.).  
*Dried sodium sulphate* ..... 3iss (45 Gm.).

M. Sig.: One-half to 1 dram (2 to 4 Gm.) in glass of hot water thirty minutes before meals.

Chase (Boston Med. and Surg. Jour., Oct. 27, 1910).

**Hexamethylenamine**, together with the other dietetic and hygienic measures, is useful in early cases of cholelithiasis, or in cases where the indications for operation are not urgent. If operation has to follow, the antiseptic action of the drug on the bile may be helpful in preventing septic

complications. Anderson (Australian Med. Jour., Aug., 1910).

A crisis of gall-stone colic requires absolute rest in bed and hot applications over the site of the gall-bladder. Friction with **methyl salicylate** is also advised. **Skimmed-milk** diet is indicated, or **kefir** made with skimmed milk. An enema of **antipyrin** and **laudanum** is sometimes useful, as well as antipyrin internally. Finally, if all else fails, morphine must be used hypodermically. Lereboullet (Paris Méd., June 1, 1912).

The writer places exclusive reliance upon **salicylic acid**. He occasionally uses **sodium salicylate** in combination with **extract of belladonna**. He credits its value not so much to any cholagogue action as to its influence on the inflammatory symptoms. Its beneficial influence is exerted in both acute and chronic cases, especially when combined, as it should be, with **rest in bed** and the application of **hot compresses**. He usually prescribes:—

**R. Acid, salicylic, or sodium salicylate** ..... gr. viij (0.05 Gm.);  
*Extract of belladonna* ..... gr.  $\frac{1}{8}$  to  $\frac{1}{4}$  (0.008 to 0.016 Gm.);

dissolved in **hot water** and given two to four times daily. The author has never observed satisfactory results from any of the much-recommended cholagogue cures. P. Mayer (Lancet, June 1, 1912).

The medical treatment should not be continued too long. The dangers from the complications mentioned are too great; especially should the practitioner be cautioned concerning *the alarming increase of cancer of the biliary apparatus that is traceable to the effect of gall-stones*.

I do not find that gall-stones and acute gastritis, as they present themselves in practice, offer any difficulty in the way of differential diagnosis. The trouble is to diagnose gall-stones from

gastric or duodenal ulcer and membranous colitis. As to direct cause of the pain of gall-stones, there is too much of the hypothetical about all the speculations on this point. The peritoneum, when inflamed or distended, is always painful. In making a diagnosis from the stools I dilute the feces and sift them through a Boas or Dudley D. Roberts stool sieve.

Occasionally we are confronted with sufferers from gall-stones who, although they undoubtedly need operation, are in too exhausted a state to stand it. Here the experience and critical judgment of the clinician comes in to ascertain if and how long the operation may be safely postponed. The metabolic cases where the operation shows no infection of the gall-bladder require careful dieting, **Carlsbad-Sprudel** or **Bedford magnesia water**. A case which may have originally been due to disturbed hepatic metabolism may later show infection of the gall-bladder.

I do not use cholagogues. There are no cholagogues except those that do harm; even the bile-salts, when so administered, injure the stomach. By the time the cholelithiasis is established it is impossible to prevent catarrhal duodenitis, because this, as a rule, precedes the catarrh of the biliary apparatus. In treating this condition, I study the feces and ascertain what foods are not digested, and exclude them, enjoin rest in bed, hot applications to the abdomen, and order a half-pint of hot Carlsbad-Sprudel water at 7 A.M. before breakfast and at 5 P.M. It is, in my opinion, impossible to dissolve the calculi, and any treatment directed toward this end is bad procrastination.

As soon as a diagnosis of gall-stones is made definitely, and the condition of the patient permits it, I recommend sur-

gical treatment, even if the gall-stones are not due to infection, but to abnormal liver metabolism; they must be removed. The surgical procedures proper are treated elsewhere in this work (see Vol. I, p. 103).

**Cholecystectomy** is not so simple or so safe an operation as **cholecystotomy**. It requires a larger incision and more extensive manipulation. There is danger of injury to the common duct and deep vessels and a considerable amount of raw surface sometimes results in the gall-bladder notch of the liver after excision, requiring special measures to check the oozing of blood. Should trouble in the shape of stricture, etc., arise in the common duct later, loss of the gall-bladder disturbs the anatomy and removes a valuable guide, and, instead of an easy, safe cholecystenterostomy for relief, the far more difficult operation, that of implanting the common duct into the duodenum, will be required. While this may be accomplished successfully with the employment of the Coffey technique, the bad general condition of such patients renders any serious operation unusually hazardous. William J. Mayo (Can. Med. Assoc. Jour., Sept., 1911).

According to the researches of Professor Aschoff, the formation of gall-stones depends on congestion in the gall-bladder and cholecystitis. Congestion without inflammation produced calculi of cholesterol which are absolutely innocuous. Gall-stones may be left undisturbed so long as no symptoms of infection are present, and if cholecystitis by infection has developed the principal aim should not be to remove the stones, but to overcome the infection. Gall-stones hold only a secondary position in the sequence of events, being not the cause but a product of the disease. Cholecystitis might terminate in recovery without the removal of the gall-stones. The writer considers that an operation might be avoided in 80 per cent. of cases of cholecystitis,

because in the great majority of instances the infection might be overcome, with the result that the disease becomes latent. The question whether a case would come into this stage of latency is sometimes rather difficult to answer and great experience is required for the formation of a reliable opinion. When the region of the gall-bladder continues to be painful between the attacks, when the temperature is rising, and when the patient's appetite, digestion, and general condition are unfavorable, little hope exists that a state of latency will develop; when, on the other hand, the pains are lessened by the administration of **castor oil** a stage of latency might follow a visit to **Carlsbad**. It depended on the mode, the degree, and the duration of the infection and its influence on the liver and the patient's general state whether surgical interference was indicated. Internal treatment is indicated (1) in acute cholecystitis and cholangitis, with the exception of gangrenous, perforating, seropurulent, and septic forms, and (2) in chronic cholecystitis showing a tendency to recovery, as well as in dropsy, obliteration, cicatrization, and calcification of the gall-bladder, but not in chronic empyema and chronic cholangitis, nor in the so-called chronic obstruction of the bile-duct. Operation is absolutely indicated in cholecystitis acutissima, in chronic cholangitis, in acute septic cholangitis, in perforation of the gall-bladder and the bile-duct, and in cancer; the question of operation is one for consideration in cases where the health of the patient is continuously affected and he is unable to work.

These indications are rather difficult to recognize. Palpation is not always reliable. In chronic cholangitis, for instance, no tumor is palpable, and an operation is nevertheless indicated; in dropsy of the gall-bladder a considerable tumor may be present, but an operation is contra-indicated. Pyrexia is absent in 50 per cent. of cases of empyema, and icterus also in 30 per cent. of cases

of gall-stones in the ductus choledochus. The clinical history is of the greatest importance. In reporting the results of his operations the speaker said that up to the present time he had performed 1866 operations on the gall-bladder and the bile-ducts; 1229 were uncomplicated cases, with a mortality of 3 per cent.; in 307 of these cases cystotomy, cystendysis, and cysticotomy were performed, with a mortality of 2.3 per cent.; 455 were cases of cystectomy, with a mortality of 3 per cent., and 467 were cases of choledochotomy and drainage of the hepatic duct, with a mortality of 3.4 per cent. In 637 cases complications existed, the mortality being 14.1 per cent. In 290 cases malignant complications were present—namely, cancer, biliary cirrhosis, and septic diffuse cholangitis, the mortality being here 78.6 per cent., so that the total mortality in cases with complications was 43.5 per cent. Kehr (*Transactions of the Berlin Med. Soc.; Lancet*, July 20, 1912).

The writer advocates operative treatment when one feels warranted to make a diagnosis of gall-stones or gall-bladder infection, provided there is no definite contraindication. Gall-stones cannot be dissolved and carried off by medical treatment, and the passage of a few stones does not mean that all have passed. When the stones are confined to the gall-bladder and its drainage not disturbed, an operation is a simple matter, but when they have passed into the common duct or are ulcerating through into the intestine, when the cystic duct has been blocked, or the small liver passages affected and jaundice appears; or when the patient has developed a chronic or an acute pancreatitis, or irritation has produced a cancer of the gall-bladder, all of which may be the result of watchful waiting or delay, it is another matter entirely. We should understand that to wait for serious symptoms is as unjustifiable as to wait for metastases in cancer. J. H. Gibbon (*Jour. Amer. Med. Assoc.*, June 13, 1914).

The indications for **cholecystectomy** are as follows: (1) in very thick, acutely inflamed, bright red or gangrenous gall-bladders due to impaction of a stone in the cystic duct; (2) in chronically thickened gall-bladders; (3) in gall-bladders much distended with clear fluid from impaction in the cystic duct; (4) whenever suspicion exists of malignant disease; (5) in chronic cholecystitis without stones, but with moderate thickening and ulceration of the mucous membrane, giving little yellow spots on the mucous surfaces, the "strawberry gall-bladder"; (6) in chronic cholecystitis without stones but with adhesions to the surrounding organs, especially the pylorus; (7) all cases of gall-stones in which the operation is not for any reason unusually difficult or dangerous; (8) all cases of cholecystitis without stones where like conditions exist. Lund (Surg., Gynec. and Obstet., Mar., 1917).

The mortality difference in the two operations—cholecystectomy and cholecystostomy—is as nothing compared to the mortality due to the local disease and general condition of the patient. One must eradicate the notion that gall-stones are the essential indications for surgery in cholelithiasis. Gall-stones are but a single sequel and by no means the most important one. Cholecystectomy in the average case will show an immediate mortality slightly in excess of cholecystostomy, but one *must* remove the gall-bladder which is the seat of hydrops or empyema, or when the cystic duct is strictured or contains an impacted stone. The strawberry gall-bladder must also be excised for permanent relief, likewise the greatly thickened or distorted gall-bladder, and the gangrenous or suppurating gall-bladder, unless the dangers of immediate removal contraindicate. In 41 cases of recurrence of symptoms the primary operation was cholecystostomy, and in 8, cholecystectomy. In 65 per cent. of recurrences after cholecys-

tostomy the cause was traceable directly to failure to remove the gall-bladder.

The recurrences following cholecystectomy are related to thoroughness and care in operation. Drainage may convert unsuccessful cholecystectomies into successful ones. In the presence of jaundice and the absence of a markedly and macroscopically diseased gall-bladder cholecystostomy is the operation of choice.

Drainage for cholangitis by the way of the gall-bladder is much more simply made than drainage by the common duct. It is true that more adhesions are found after cholecystectomy than cholecystostomy in cases reoperated. Subsequent dilatation of the common duct and the stump of the cystic duct was not met by the author in over 1800 operations.

The writer inclines now to cholecystectomy when the gall-bladder is obviously diseased, this covering the vast majority of all cases. When the infection is more distinctively cholangitic and intrahepatic, as evidenced by minor appearances of inflammation of the gall-bladder with thickening, enlargement and a "streaky" appearance of the liver, or when the major lesion is in the pancreas or common duct, he prefers to leave the gall-bladder, using it either for internal drainage by cholecystoduodenostomy or for prolonged external drainage by cholecystostomy. J. B. Deaver (Surg., Gynec. and Obstet., Mar., 1917).

The 4 chief dangers that may threaten the life of the carrier of gall-stones are: 1, acute suppurative or gangrenous cholecystitis; 2, cholangitis; 3, malignant disease of the gall-bladder; 4, operation in delayed cases. In the severer types of acute suppurative or gangrenous cholecystitis operation should not be delayed. **Simple drainage** of the gall-bladder is the operation of choice in these cases. Cholangitis usually implies that 1 or more gall-stones have entered the common duct and caused stoppage of the flow of bile, with re-

sulting infection. The choice of the time for operation in these cases is a matter of judgment on the part of the surgeon. Operation is more hazardous at the height of the attack and in the presence of jaundice, but if the symptoms persist more than 48 hours and the patient's general condition is growing worse from the absorption of septic bile, operation offers the best chances and should not be further delayed. B. T. Tilton (N. Y. Med. Jour., Jan. 1, 1921).

As to the direct indications for operation all signs are misleading in these cases, but (1) fever, (2) constant and extreme tenderness over the liver, and (3) leucocytosis are the most reliable signs of suppuration. The mortality in those cases which I was obliged to treat medically is much greater than those submitted to the surgeon, as cancer often supervenes in cases treated medically.

Case of his own from Enderlen's clinic, 1 of Enderlen's, and 6 by other surgeons of recurrence of gall-stones with a silk suture inserted at the previous operation for a nucleus. In order to avoid this, the writer advises that either catgut be used or that if silk be used, it be left long, so that it may be removed. Flörcken (Deut. Zeit. f. Chir., Bd. xciii, H. 3, 1908).

Analysis of 209 articles published on cholelithiasis during the last five years shows that the operative treatment should include steps to avoid recurrence. Stones left behind, adhesions, hernias, and strictures of the bile passages [and silk sutures left behind] are not rare. Actual recurrence of stones is exceptional after removal of the gall-bladder, and all the evidence is in favor of this as the best, although the most dangerous, procedure. To avoid the pseudorecurrences, the neighboring organs should be carefully examined to ascertain if there is not some other morbid condition capable of causing such. A. Exner (Centralbl. f. d. Grenzgeb. der Med. u. Chir., Bd. xv, Nu. 3, 1912).

Out of 147 personal cases, 13.6 per cent. sustained relapses or received no apparent benefit from the operation. Of the remainder 64.6 per cent. recovered fully, while 19.7 per cent. recovered partly, but were efficient for work. The best results occurred when the stones were present in a sacculum or reservoir in which cholecystitis had developed. The results of total extirpation are most favorable. Spurious recurrence is apt to occur when stones form in the liver. After cholecystotomies about one-half the cases give no further trouble as far as overlooked or recurrent stones are concerned. In the others the symptoms are due to adhesions, sclerosis, etc. It is therefore best in all cases of cholecystitis to extirpate the gall-bladder. Arnsperger (Münch. med. Woch., Jan. 9, 1912).

The ductus choledochus should be drained after cholecystectomy when there is: 1, thickening of the pancreas, especially of the head; 2, when the ductus choledochus is thickened and distended; 3, when there is a history of icterus, chills, and passing of stones; 4, when a considerable amount of the cystic duct is left and it is ruptured to the common duct; 5, when many small stones are found in the gall-bladder and the cystic duct, suggesting the presence of similar ones in the common duct; 6, drainage of the hepatic duct when cloudy pus oozes from the stump of the cystic duct, proving that there is infection of the choledochus; 7, in the presence of liver enlargement, indurated liver, and cirrhosis. J. B. Deaver (N. Y. State Jour. of Med., Sept., 1912).

The writer, after an experience based upon 300 operations upon the gall-bladder and bile ducts, makes a plea in favor of saving the gall-bladder in at least a majority of the cases. He had never seen an empty or collapsed gall-bladder when examining it during the course of operations in the upper abdomen. The fact that it was always filled with bile goes to prove that it has much to do with

keeping up and regulating the pressure in the bile ducts and liver. This post-operative effort of nature to reproduce the gall-bladder is evidence that the gall-bladder not only has the function of storing bile, but also has a pressure regulation function upon the biliary system. These facts should be taken into consideration where the question of cholecystectomy versus cholecystostomy is to be decided. When should cholecystectomy be resorted to? (1) In all cases of hydrops with stricture of the cystic duct. (2) Many cases of acute gangrene or threatened gangrene of the gall-bladder. (3) All cases complicated with embedded stones in the cystic duct with ulceration produced by contact with the embedded stone that when healed would probably cause stricture. (4) All very thick walled gall-bladders due to fibrous or calcareous degeneration. (5) All cases of ulceration due to pressure of large stones. (6) In cancer of the gall-bladder where the disease is limited to the gall-bladder. W. H. Magie (Trans. Western Surg. Assoc.; Med. Rec., Feb. 8, 1919).

To diet these patients guardedly, examining the feces carefully, is the first rule. But there are no hard and fast, cast-iron dietetic *régimes*. The rule to follow is to study and find out what agrees the best. After the operation the Carlsbad waters are very effective in preventing recurrence. A recurrence of the stones, gastritis, enteritis, and colitis are the commonest complications. The best prophylactic for those who are inclined to gall-stones is **Carlsbad-Sprudel** or **Bedford water**, as hot as it can be drunk, and living on such a diet as has proven itself to be best digested according to the methods above referred to.

**Sulphur waters** increase and dilute the bile and greatly excel the alkaline springs. The patients may drink the water at home or, preferably, should

spend a few weeks at some watering-place where strong sulphur springs exist. The cure should be continued for some time after the expulsion of the stones. The excessive ingestion of eggs is a possible etiological factor in causing gall-stones, since the yolk contains as much as  $\frac{1}{2}$  per cent. of cholesterolin. Hence **eggs** and also **bread** should be used in moderation. A. Winckler (Therap. Monats., May, 1900).

To ward off gall-stone trouble it is necessary: 1, to avoid or attenuate infection of the biliary passages; 2, keep the composition of the bile normal; 3, to maintain a copious secretion of bile, and, 4, to insure its constant excretion. The meals should be frequent and light. The extractives have the property of promoting the passage of the bile into the duodenum and consequently a glass of consommé or something of the kind should be taken just before retiring. A little milk might be sipped if one wakes in the night. By thus preventing the stomach being long empty at a time, the contraction of the gall-bladder is promoted and the circulation of the bile kept active. Dufourt (Presse méd., vol. xiv, No. 22, 1906).

It is very important to promote the expulsion of the stagnant, thickened bile. This can be effected by making the bile more liquid. A thinning of the bile is without doubt produced, and in a less harmful fashion than by cholagogues, by **drinking abundance of water**. The water is best given on an empty stomach, and as hot as possible; cold liquids should be strongly forbidden, as they frequently induce attacks of colic. The patient should drink in bed in the morning about an hour before breakfast 1 to 2 tumblers of **hot water**, in like manner a tumbler in the evening before going to bed, and smaller quantities frequently during the day. It is also very useful to take warm water at mealtimes. Patients easily become accustomed to this, and experience the less objection to the

warm water the hotter they drink it. A dilution of the bile can also be effected through the rectal injection of water. The introduction of large quantities of water into the intestines has been recommended in cholelithiasis for about thirty years, and many authors have confirmed its useful action. For a long time in Carlsbad **enemata of Carlsbad-Sprudel water** cooled down from 40° to 50° C. have been employed, the patient retaining them as long as possible up to an hour. These injections prove especially useful in chronic jaundice (obstruction of the common duct), and are to be recommended also in such cases when the administration of large quantities of water by the mouth does not appear advisable on account of a coexisting atony or dilatation of the stomach. They are, moreover, of special value where catarrh of the intestine is present at the same time, this condition being, as is well known, a relatively frequent accompaniment of cholelithiasis. Paul Mayer (Lancet, June 1, 1912).

#### Duodenal Intubation and Lavage.

—There are two conditions in which non-operative treatment is effective and in its proper sphere: 1, as a prophylactic where one or more attacks of catarrhal icterus have already occurred, and, 2, in cases that have already been operated and where the symptoms of cholelithiasis again appear. For these conditions **duodenal intubation and direct lavage of the duodenum** are advocated.

[As to duodenal intubation and lavage in the treatment of catarrhal jaundice, I described it in 1895 (Johns Hopkins Hosp. Bull., April, 1895). The same method was more completely described in the Archiv f. Verdauungskrankheiten, Bd. ii, S. 85. This was the first method of the kind proposed for the diagnosis and treatment of duodenal diseases. (See also Hemmeter's work on "Diseases of the Intestines," vol. i, pp. 264-267.) The method was subsequently improved by Franz Kulin (Archiv

f. Verdauungskr., Bd. iii, S. 19). In 1911, M. Gross, of New York, and Max Einhorn published still more feasible and practical methods, so that I eventually deserted my original method of 1895 first for that of Kuhn and later for the instruments of Gross and Einhorn. The entire history of the discovery of this method is presented in a polemic between Einhorn and myself which runs through vol. xvii of the Archiv f. Verdauungskrankheiten during the year 1911. Though adverse to controversy, I felt it my duty in the interest of historical accuracy to prove the priority of my discovery and use of this method, which has rendered the duodenum as accessible to direct investigation and treatment as was hitherto the stomach. And although the instruments may be modified and improved, it is the first pathfinder which is acknowledged as the pioneer of the original idea, not those who later simply improve the method. J. C. HEMMETER.]

Simple catarrhal icterus is in most cases the consequence of acute or subacute gastroduodenal catarrh. Either the *porus biliaris* is swollen or occluded by tough mucus or the duodenitis has actually extended to the biliary passages. As these are quite narrow, a very slight swelling of the mucosa suffices to prevent the exit of the bile.

[Pel believes that some cases of simple catarrhal icterus are due to an unknown infective agent, because he was unable to assign any dietetic error or previous gastritis as the cause (Pel: "Die Krankheiten der Leber und Gallenwege," S. 296). He deems this view confirmed by the occasional epidemic occurrence of catarrhal icterus—numerous cases at the same time in the same locality. Personally, I have records of 6 cases of catarrhal icterus in which the stomach and duodenum were found normal to the most thorough clinical investigation, which would suggest not a stenosis of the gall-ducts due to catarrh, but a cholangitis due to local infection. The typhoid and the colon bacillus are mentioned as the microbic agents. These



facts are mentioned to prove that not every case of so-called catarrhal icterus is really this, but may be an infection.

But my main object is to call attention to the effect of direct lavage of the duodenum by duodenal intubation in catarrhal jaundice. J. C. HEMMETER.]

If the diagnosis is correct and the jaundice is not due to something graver, it will subside in from eight to nine days by duodenal lavage with Einhorn's or Gross's tube. My favorite solution is hot **Ringer's solution** (NaCl, CaCl, KCl). Where the fluid comes back containing much mucus about 3 Gm. (45 grains) of sodium bicarbonate are added to about 500 c.c. (1 pint) of Ringer's solution. The most available disinfectant is **dilute hydrochloric acid**, 3 parts to 1000 ( $\frac{3}{10}$  of 1 per cent.). When this is done after the duodenum is clean the icterus subsides in about a week. **Aluminum silicate** (kaolin) was used by me in 2 cases in form of a suspension, with apparent benefit: Twelve Gm. (3 drams) of aluminum silicate in 1 pint (500 c.c.) of warm salt water.

It must be emphasized that by means of duodenal intubation the patient can be fed directly into the duodenum in case absolute rest is desired for the stomach, but, further than this, liquid food, for example, milk and eggs beaten up in milk, can be injected directly into the jejunum, so that the presence of food in the duodenum can be avoided. As the great majority of these duodenal catarrhs are merely extensions from a pre-existing gastritis (assuming that there is a genuine catarrhal duodenitis and not an infection), dietetic rest of the stomach in this type of icterus is an important factor in recovery. As regards icterus de-

pending on duodenitis, its importance depends upon the fact that this train of pathological events is a condition in the pathogenesis of gall-stones. We must learn to look far back in the connection of pathological events when we are dealing with such subtle and complex abnormalities.

After some experience the introduction of the **duodenal tube** is an easy matter. In the main, the duodenal tube is simply a direct prolongation of the stomach-tube. The method of introducing the tube enables us, to a great extent, to exclude the function of the stomach during the entire procedure, reaching the pylorus over the shortest route and in the shortest time. The principle of non-interference with the gastric function is still more pronounced in cases where the stomach is displaced or dilated. In many cases the duodenum may be reached in half an hour or less, and there are even cases in which the small, heavy ball practically drops right into the open pylorus. As a matter of course, it is necessary to see to it from the start that there is a "free" outflow, meaning that the duodenal contents will flow almost uninterruptedly into the lower-lying receptacle. This is effected, if measures to that effect be necessary, by occasional aspiration. The technique is given as follows: The patient swallows the tube, which is weighted with a small perforated silver ball, and assumes the right recumbent position. This tends to gravitate the small ball toward the pylorus, drawing the tube with it. When it has arrived there, the farther propulsion of the ball may be left to the mechanism of the pyloric part of the stomach. It is only by the aid of the "duodenal tube" that the desirable elucidation on the function of this section of the digestive tract can be obtained,—elucidation especially on the external secretion of the pancreas, all previous knowledge on the point having been gained

by animal experiment, that is, on wounded and, therefore, pathological animals. The chemical examination of the duodenal contents obtained from 30 patients yielded the following results: 1, average quantity obtained, 32 c.c. (1.06 ounces); 2, average consistency, viscous; 3, average transparency, transparent; 4, average color, light green; 5, average reaction on litmus, strongly alkaline; on phenolphthalein, always acid; 6, average specific gravity, 1.006; 7, average quantity of mucin, 6.7 per cent. volume; 8, amylase and steapsin, the starch and fat-splitting ferments, were never entirely absent in fresh duodenal juice; 9, the average values for trypsin were between distinct and weak, and were totally absent only in 2 cases. Having thus established average values, it will be possible to determine deviations in future examinations. Gross (Boston Med. and Surg. Jour., July 13, 1911).

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**CHOLERA, EPIDEMIC.** See  
INTESTINES, DISEASES OF: CHOLERA  
ASIATICA.

**CHOLERA INFANTUM.**—  
**DEFINITION.**—A particularly grave form of infantile diarrhea, with symptoms closely resembling those of true cholera; frequent and often persistent vomiting, copious serious dejections, high fever, and a rapidly developing condition of profound collapse.

It is a comparatively rare disorder, forming not more than 1 per cent. of all the diarrheal cases met with during the summer months. Unfortunately for the accuracy of our statistics the term has been applied indiscriminately to all cases of severe infantile diarrhea. In the opinion of the best writers the name should be limited to those cases only which are characterized by intense choleric form symptoms.

**ETIOLOGY.**—The exact nature of cholera infantum is still uncertain. As yet pathologists have not been able to connect it with any specific form of intoxication, but analogy points strongly to its being a toxic condition produced by absorption from the intestinal tract of a specific toxin, associated with the imperfect digestion of impure milk. The prolonged heat of July and August appears to be a distinctly predisposing factor. Infants living under faulty hygienic conditions, and supplied either with an injudicious dietary or with milk food in the preparation of which due care has not been taken, and which has been allowed to stand for many hours in a heated and impure atmosphere, appear to be among those most prone to attack. Although the disease may develop suddenly in the comparatively healthy, we find that, in the majority of cases, there has been a more or less severe antecedent disorder of the gastrointestinal tract.

In a room kept at a temperature of 27° or 28° C. (82° F.) for the use of the prematurely born, instead of individual incubators, other infants sometimes kept therein were found by the writer to all develop diarrhea. This suggests that the heat alone—aside from the nature of the food—may have a direct injurious action on young children. In the homes of the poor in summer this temperature of 28° C. (82° F.) is often surpassed. Rietschel (Monats. f. Kinderheilk., April, 1910).

According to L. Emmett Holt, in 2000 cases of deaths among children from summer diarrhea, it was proved on investigation that only 3 per cent. were breast fed, revealing a most extraordinary immunity among infants nursed by their mothers. Niven, of Manchester, published statistics of infant diarrhea in the summer of 1896 in that city. Out of 500 deaths, only 15 were being breast fed when

taken ill. The relative chance of dying from diarrhea of hand-fed as compared with breast-fed children was as 8 to 1 under 1 month old, 95 to 1 at 1 month, 125 to 1 at 4 months. These figures coincide with those of Holt, viz., 97 per cent., while Minert, of Bavaria, finds the rate in his country to be 96 per cent. Editorial (Pediatrics, July, 1911).

**PATHOLOGY.**—There are few changes found after death, either in the intestinal canal or in any of the organs. The only lesion present is a desquamative catarrh of the gastrointestinal tract. The kidneys are paler than usual, with moderate cloudy swelling of the cortex, but not to an extent greater than may be present in other febrile disorders of infancy (Holt). The early symptoms may, therefore, be ascribable to the influence of some toxin upon the heart, nerve-centers, and vasomotor nerves of the intestines, while many of the later symptoms must be referred to the great abstraction of serous fluid from the body.

**SYMPTOMS:**—After a variable, but generally brief period, characterized by restlessness, abdominal discomfort, and a rapidly rising temperature, the infant begins to vomit, and simultaneously, or shortly afterward, purging commences. The vomiting recurs frequently. At first the stomach contents only are ejected; then a bile-stained mucus, and, lastly, nothing but a serous fluid. The evacuations from the bowels soon assume the same serous character. They lose their fecal appearance and acid reaction, and consist almost entirely of a colorless fluid, copious in amount, alkaline in reaction, and of a peculiar musty odor. Examined microscopically little has been found in this fluid beyond a large amount of epithelial *débris*, some cells, and numerous

bacteria. These discharges soak into the diapers, leaving little stain and scarcely any fecal matter to indicate that the fluid has come from the intestines. Although these evacuations are very frequent, recurring every half-hour or hour, pain is not generally a marked feature.

The temperature, taken in the rectum, is always elevated, generally between 104° and 105° F.; nevertheless, the body feels cool to the hand. Thirst is extreme, but liquids and food of all kinds are rejected shortly after they are taken. With such a drain upon the fluids of the body the infant rapidly loses weight and strength, and in a few hours becomes greatly altered in appearance. The face is of an ashy pallor, the eyes sunken, the features pinched, and the expression anxious. The fontanelle, if open, is much depressed; the pulse is rapid and weak, sometimes intermittent; the urine is scanty, and in severe cases appears to be altogether suppressed.

During the earlier hours of the disease restlessness is a marked symptom; but, as the strength fails, this is replaced by a condition of apathy, which, later on, may develop into the hydrocephaloid state, the spurious hydrocephalus of older writers. With the development of this condition the head becomes retracted, the child drowsy, the pupils sluggish and sometimes unequal, the abdomen sunken or retracted, and respiration uneven and sighing; sometimes it may have a Cheyne-Stokes character. Not infrequently twitching of the arms and legs may be noticed. Toward the end the infant either becomes more comatose, or an attack of convulsions may supervene and usher in the close.

In some cases a condition of hyper-

pyrexia may precede the fatal termination. In others the high temperature of the earlier hours may pass away and a more moderate pyrexia, or even a normal temperature, take its place. Nevertheless, if the graver symptoms of collapse persist, this fall in temperature must be regarded as an unfavorable omen.

The course of this disease is very rapid, terminating in many cases in collapse and death within twenty-four or forty-eight hours after its commencement. Should hydropneumothorax symptoms set in, the end may be delayed for a day or two longer. In the few cases which go on to recovery, cessation of vomiting is often one of the earliest symptoms of improvement; then gradually the character of the stools alters, becoming more fecal; the restlessness abates, and improvement takes place in the pulse and general appearance of the infant. Convalescence, however, is always tardy, and relapses are not uncommon.

**DIAGNOSIS.**—The character of the onset, the persistent vomiting, the profuse serous or rice-water dejections, the high temperature, and the symptoms of profound collapse, rapidly developing within a few hours, form a picture unlikely to be mistaken for any other condition.

**PROGNOSIS.**—Few diseases have a worse prognosis. The higher the rectal temperature, the younger the infant, the hotter the weather, and the more unhygienic the surroundings, the more hopeless is the case. Rotch considers the disease to be to some extent self-limited, and says that if the infant survives the first three days the prognosis improves.

**TREATMENT.**—Regarding the disorder as a toxic condition due to the

absorption of a poison from the alimentary canal, our first efforts must be directed to clearing out this tract as promptly and thoroughly as possible. Drugs are of little value. As soon as practicable the stomach should be thoroughly washed out with a tepid solution (1:100) of sodium chloride or bicarbonate. Following this the whole tract of the colon should be irrigated with normal saline solution. To insure passage of the solution into the higher portions of the colon, the hips of the infant must be well elevated, and the tube passed well up into the bowel. The solution should be allowed to run into the gut in a gentle, steady stream from a fountain syringe placed at a height not exceeding two feet. The passage of the fluid upward may be favored by gentle massage along the course of the bowel. The temperature of the irrigating fluid (85° to 100° F.) will be determined by the condition of the patient and the degree of pyrexia. These irrigations should be repeated frequently.

The use of any antiseptic in the solution for irrigating is, in our opinion, not to be recommended. To be in any degree effectual such antiseptic must be employed in an efficient strength, and from such solution there is always danger of poisonous absorption. Whisky or brandy, however, may always be added to enemata if thought desirable.

Bismuth in large doses is often recommended, but unless given with an antiseptic, has never seemed to the writer to have the slightest effect in allaying the irritability of the stomach or arresting the purging. The use of the salicylate of lime was advocated by Walter Kilner. The writer prefers to give the salicylate of bismuth, made by combining carbonate of bismuth with salicylate of soda, as in the following prescription:

**R. Bismuthi subcar-**

*bonatis* ..... gr. x (0.6 Gm.).

*Sodii salicylatis*.. gr. j (0.06 Gm.).

*Glycerini* ..... ℥xv (1 c.c.).

*Aque* .... q. s. ad f3j (4 c.c.).

M. Sig.: To be given every four hours (to a child 6 months old).

Another drug to which great value has been attached is the **bromide of potassium**. It is said, in doses of 7 or 8 grains (0.45 or 0.5 Gm.) every two or three hours, to produce a rapid improvement in the number and frequency of the stools. Eustace Smith (Pediatrics, May, 1912).

No form of nourishment should be permitted to be given by the mouth during the first twenty-four hours. The digestive functions of the stomach and duodenum are in complete abeyance, and any food administered will either be at once rejected by the stomach, increasing its hyperemic condition, or, if retained, will go on to fermentation.

With **albumin milk** properly given complete recovery may virtually be guaranteed. The infant suffering from diarrhea and vomiting is given nothing but tea for from 12 to 24 hours, no longer, and then the albumin milk begun with 5 Gm. (75 minims) 10 times a day, with 3 per cent. of a maltose-dextrin mixture. The amount of albumin milk is increased by 50 Gm. (12½ drams) each day until the daily ration totals 300 Gm. (10 ounces). After the weight has become stationary, carbohydrates can be added up to 5 per cent. of the maltose-dextrin mixture. In a child over 3 months old, 1 or 2 per cent. flour or oatmeal can be added. Langstein (Therap. Monats., Aug., 1915).

To counteract the depressing action of the poison and to prevent the parietic condition of the intestinal vasomotor system, a hypodermic injection of **morphine**, combined with **atropine**, is probably our best remedy. For an infant 1 year old an initial dose of ¼<sub>100</sub> grain of morphine and ¼<sub>1000</sub> grain of

atropine may be given immediately after the intestinal lavage. The morphine may be repeated in an hour if the desired sedative action is not obtained.

For a child a year old, ¼<sub>30</sub> grain (0.002 Gm.) of **morphine** may be used, combined with 5 or 6 drops of **ether**; and the injection may be repeated in an hour's time if the symptoms continue. Eustace Smith (Pediatrics, May, 1912).

In conditions of drowsiness or stupor the use of morphine is contraindicated. In these cases **camphor** dissolved in oil and **strychnine** will both prove of service as cardiac and respiratory stimulants, and should be given hypodermically. Their effect should be watched, and the injections repeated every four or six hours as may be found necessary to secure the desired stimulation. Drugs by the mouth should be avoided, as doubt must exist as to the rapidity and to the extent of their absorption.

For the pyrexia **baths** are demanded, and should be given with discretion and care. Cool baths in a depressed state of the infant, when the extremities are cold and the pulse lagging, must be used cautiously, even although the temperature in the rectum may show considerable pyrexia. The bath at the outset should have a temperature of 95° F., and may be gradually cooled till a temperature of 80° or 85° F. is reached. The infant should remain in the bath from five to fifteen minutes, according to the effect produced, and while in the bath brisk **friction** should be employed over the limbs and body generally. A prolonged **warm bath** at 98° F. or a **hot mustard bath** by stimulating the superficial circulation will often do good. Sometimes a **cool half pack**, with **heat to the extremities**, acts well.

To counteract the effects of the drain of fluids from the tissues, no method can be compared with the injection into the cellular tissue of 6 or 8 ounces of a sterilized **normal saline solution**; it can most conveniently be injected into the subcutaneous tissue of the thigh, abdomen, or buttock, and may be repeated twice a day or oftener. Marked improvement in all the symptoms generally follows its employment. A suitable syringe can easily be made by attaching a hypodermic needle to the nozzle of a Davidson syringe by means of a few inches of rubber tubing.

Hydrencephaloid symptoms call for the free use of stimulants; but opium, in this condition, is better avoided. During the course of the disease care must be taken to maintain due warmth in the extremities. **Sinapisms** over the stomach may be of occasional benefit.

(See also DIARRHEAL DISORDERS OF CHILDREN and NURSING AND ARTIFICIAL FEEDING.)

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**CHOLERA MORBUS.** See INT-  
TESTINES, DISEASES OF: CHOLERA MOR-  
BUS.

**CHOLURIA.**—This is a morbid condition of the urine observed in jaundice and characterized by the presence in it of the constituents of the gall, especially the bile-pigments and the bile-acids.

In urobilinuria the normal constituents of the bile are not found in the urine, but a derivative of the bile-pigments—the urobilin—is found instead.

**SYMPTOMS.**—Although the bile-acids are ordinarily present in the urine in choluria, they do not occasion characteristic symptoms, and can only be revealed by special tests. The presence of the bile is more easily detected.

The urine containing bilirubin exhibits a color varying from a light saffron-yellow

to one resembling mahogany or porter; even when the color is dark brown or almost black, the urine will show a tinge of olive-green or green-brown when it is seen in thin strata. The color of the urine may resemble that of a very concentrated urine or of urine containing blood; in the later cases the froth of the urine is white, while the froth of the icteric urine is yellow and tinges white a piece of linen or blotting-paper dipped into it.

On standing, icteric urine ordinarily becomes greenish, because the bilirubin, by oxidizing, changes into biliverdin; by further decomposition of the urine the pigments are further changed into biliprasin and bilifuscin.

Although cholesterol is a normal constituent of the bile, it is not found in the urine in choluria, but in other morbid conditions of the urine: *e.g.*, chyluria.

**DIAGNOSIS.**—Different remedies may give the urine a color resembling that observed in choluria. When santalin, thallin, rhubarb, or picric acid have been ingested, the urine and its froth will present a yellow color. In poisoning with the fruit of *Cytissus laburnum* a dark-green color of the urine is observed, whereas it is blue-green after the ingestion of methylene-blue. The presence of the bile-pigments is revealed by different tests.

1. **Gmelin's test** consists in bringing strong nitric acid containing some nitrous acid in contact with the urine; if bile be present, a play of color is developed from green to blue, violet, and finally red. These changes are due to the gradual oxidation of the bile-pigments. The green color is the most characteristic, being dependent on the formation of biliverdin. It must be remembered that in most urines a reddish tint is brought out by nitric acid, while, if much indican is present, a blue or violet color may be developed.

Gmelin's test is best performed by pouring a few cubic centimeters of nitric acid in a test-tube or a conical glass; the urine is then allowed to flow gently so as to cause it to fall on the surface of the acid. The play of color is then observed at the junction of the liquids. The urine may also be placed in the tube first and the acid poured in gradually so that it sinks down to the bottom. Only the green color is evidence

for the presence of bile-pigment, since the other colors may be due to the action of the acid upon the normal urine-pigments. The presence of albumin is of no consequence; the green color is even more visible against the white albuminous deposit. Gmelin's test has been modified in different ways.

Rosenbach proposes to filter the urine through white blotting-paper and place a drop of nitric acid on the filter while still moist, or a drop of the urine and of the acid are placed separately on a white porcelain surface and allowed to come in contact. In both cases the characteristic color-rings will appear.

Gmelin's test is very reliable when the quantity of bile-pigments is not too small; when this is the case, however, it is necessary to isolate the pigment by gently shaking the urine with chloroform; this agent will dissolve the bilirubin and cause a yellow color. When the test-tube is left quiet for some minutes the chloroform solution of bilirubin will sink to the bottom, the urine can be poured out, and the test performed with the chloroform solution. Indican is not dissolved by chloroform.

Different oxidizing substances have been used instead of nitric acid.

**2. Iodine test (Smith-Maréchal):** When a few drops of tincture of iodine are added to urine containing bile-pigment an emerald-green color will appear. A watery solution of bromine will produce a similar effect.

**3. Huppert's test:** A solution of ammonia and chloride of calcium is added to the urine. When bilirubin is present a deposit of bilirubin-chalk will be formed, which is filtered and washed down in a test-tube together with strong alcohol containing sulphuric acid. When boiled the liquid takes a blue-green or emerald-green color.

**4. Jolles's test:** Jolles recommends the following method: To 50 c.c. of urine, a drop of hydrochloric acid, chloride of barium in excess, and 5 c.c. of chloroform are added. The mixture is shaken and left standing for ten minutes, then poured out and the chloroform heated in a water-bath; 3 drops of sulphureted sulphuric acid containing one-fourth of its volume of

fuming sulphuric acid are added. The characteristic rings are found at the bottom of the tube.

**5. Ehrlich's test:** When only bilirubin is to be revealed the sulphodiazobenzol test of Ehrlich may be of use. The reagent and diluted acetic acid are added to the urine. When the mixture becomes dark, a few drops of glacial acetic acid will bring out the characteristic violet color.

The biliary pigments in the urine may decompose by standing, and then the above-mentioned tests will be without result. Bilifuscin, which is formed by decomposition of the bilirubin, is revealed by moistening white blotting-paper with the urine; the paper will assume a brown color.

Urobilin is dissolved by chloroform, and the solution takes a greenish, fluorescent color upon the addition of iodine and caustic potash. Von Jaksch recommends the test of Huppert: when urobilin is present the deposit is red-brown and becomes brown or gray-brown by boiling with sulphuric acid.

**Pettenkofer's test:** The bile-acids are detected by means of this test, which depends on the development of a deep-purple color when these acids are acted upon by cane-sugar and strong sulphuric acid. This reaction is, however, for several reasons, most unreliable when applied to urine, and the bile-acids must be separated from the urine by a complicated method before the original Pettenkofer test can be made.

Strassburger, therefore, has modified the test in the following manner: Cane-sugar is added to the urine, and the solution is filtered through white filtering-paper. After drying the filter a drop of strong sulphuric acid is placed upon it, and after one-half minute a beautiful red color will appear if bile-acid be present; the color finally changes into a dark purple.

#### ETIOLOGY AND PATHOLOGY.—

Choluria takes place when the constituents of the bile are absorbed by the lymphatics and pass into the blood-vessels, from where they are excreted by the kidneys. It is, therefore, a constant symptom of jaundice, and is often observed before either the skin or the mucous membranes get stained with bile-pigment. The conditions which give rise to icterus will be dis-

cussed elsewhere, but by the examination of the urine it will never be possible to discover the origin of the jaundice. In some cases the pigment contained in the urine does not seem to be due to absorption of bile in the liver, but to have been formed directly by decomposition of the blood-pigments, either while circulating in the blood (hematogen icterus) or after the blood has been extravasated in the tissues (Quincke's inogen icterus).

#### PROGNOSIS AND TREATMENT.—

As choluria is only a symptom of absorption of bile by the blood, its prognosis is in close relation to that of the disease acting as cause. Even if the choluria is very considerable, it will quickly disappear when the obstacles for the regular flow of the bile are removed. The treatment must also be directed against the fundamental disease, while the symptom, choluria, needs no special treatment. I..

**CHOREA. — SYNONYM. —** St. Vitus's dance.

Some confusion arises from the fact that under the name "chorea" are included several forms of nervous disease and degeneracy having as their common and characteristic symptom jerky, arrhythmic, involuntary, inco-ordinate, muscular movements, while differing widely from one another in nature, causation, pathology, prognosis, and general symptomatology. This confusion is further added to by the varying opinions held by those who write upon the subject as to what conditions shall and what shall not be included among the choreas.

The following forms are described:—

1. *Sydenham's chorea*. With several varieties, as "chorea insaniens," "hemichorea," etc.
2. *Endemic chorea*.
3. *Electric chorea*.
4. *Hysterical chorea*.
5. *Saltatory spasm*.
6. *Oscillatory spasm*.
7. *Tic co-ordiné*, or "*habit spasm*."

8. *Posthemiplegic chorea*.

9. *Chronic adult chorea*.

10. *Huntingdon's chorea*.

Of these, the first in order is the common St. Vitus's dance, chorea minor, or acute curable chorea, and much the most common and important of the choreoid diseases. It is the form meant when the word chorea is used without qualification. Those included from the second to the seventh belong to the functional neuroses, and may be regarded as expressions of neurodegeneracy. The eighth, ninth, and tenth are attended by degenerative changes in the cortex cerebri, or spinal cord, or both.

#### SYDENHAM'S CHOREA.

**DEFINITION.**—This is the well-known "St. Vitus's dance," an acquired functional neurosis, occurring during the middle and later periods of childhood, being rarely seen before the age of 5 years and after puberty; it is more common in females than in males, is more frequently met with in urban than in rural populations, and during the spring months.

The distinction between Sydenham's chorea and St. Vitus's dance of the Middle Ages should be fully understood. The latter presented wild, dancing, involuntary movements, which developed in its victims a state of ecstasy. This ecstatic dance exerted a strong impression upon the minds of the patients, so that the disease as a mental contagion became widespread. This led to the appreciation of the condition as a severe form of St. Vitus's dance, which was called chorea Germanorum or chorea magna. The disease today described as St. Vitus's dance, or chorea minor, was first described by Sydenham, and is a disease of young people, 75 per cent. of the cases occurring between the years of 6 and 15, two-thirds of the patients being young girls. F.



Viedenz (*Archiv f. Psychiatric u. Nervenkrankheiten*, Bd. xlv, Heft 1, 1909).

**SYMPTOMS.**—The onset of the disease is often foreshadowed by symptoms covering a prodromal period of a few days to a few weeks. These premonitory symptoms consist in general nervousness, a tendency to fidget and uneasiness, a change in disposition; irritability and emotional weakness, headache, vague pains, some impairment of general health, and possibly the occurrence of some one of the acute diseases or unfavorable circumstances enumerated below as exciting causes of the disorder. The disease always develops gradually and with varying rapidity in different cases, the onset being marked by the appearance of the characteristic choreic movements. These are peculiar, jerky, often lightning-like, clonic spasms, involving the muscles of the face and head, neck, trunk, and extremities, usually more pronounced in the face and arms, and often more pronounced in one lateral half of the body ("hemichorea," when typically shown). The movements are sudden in onset and as suddenly cease; they are irregular in force and direction, markedly inco-ordinate, and differ in character from any other form of abnormal motor discharge known. They result in sudden grimaces and facial twitchings; sudden closure and opening of the eyes or mouth; sudden seizure and immediate dropping of any object it is attempted to grasp; twisting movements of the arms; peculiar dancing and bobbing movements of the feet, all of these movements seeming at times semipurposeful, leading to the idea on the part of the onlooker that they are due to bad habit or awkwardness, and could be prevented.

The movements vary in intensity from slight, scarcely noticeable twitchings of co-ordinate groups of muscles, occurring at intervals, to violent and almost continuous clonic spasmodic contractions of nearly or quite all of the voluntary muscles of the body, resulting in writhings and contortions which completely incapacitate the patient and render necessary confinement to bed. The movements may occur when the muscles are at rest, but they are often precipitated or intensified by voluntary muscular effort of any kind. They are increased by efforts to prevent them and by anything which directs attention to them. They cease entirely during sleep. In many cases speech is affected in consequence of implication of labial muscles and tongue, giving rise to peculiar jerking out of words, explosive utterances, hesitation, or indistinctness of articulation which may in some cases amount to entire inability to talk. The lips are occasionally bitten; the tongue rarely. The muscles of respiration may become involved, in which event there will be uneven, irregular respiratory movements, with, possibly, sighing, moaning, or other involuntary inarticulate sounds.

The respiratory symptoms in chorea are important. They are best observed with the thorax entirely exposed, the patient in the supine position with the trunk and limbs in position to afford the most complete bodily reaction. Points to which the writer calls attention are: "1. Irregular breathing, which is probably due to two factors, (a) lessened amplitude in some movements and increased amplitude in others, giving the impression that no two respiratory excursions are equal; (b) sudden halts or "cogs" occurring (usually singly) during inspiration or expiration, but most frequently during the latter. These do not occur in every respira-

tory movement, but are of frequent occurrence and appear to be due to a sudden arrest of the movement in one phase by the development of an incomplete movement of the opposite phase, but the original movement usually goes on to completion. These cogs render the respiratory movements distinctly jerky and may well be called choreic inspiratory and expiratory cogs. An inspiratory cog occurs most frequently near the end of expiration and an expiratory cog near the end of inspiration. 2. Now and then a sudden deep inspiration occurs, far exceeding in amplitude the usual unequal inspiratory movements, and is succeeded by a sudden explosive (forced) expiratory movement, the whole differing essentially from a sighing respiration by its rapidity in its every phase and by the absence of a pause at the end of expiration. 3. Relative decrease in the length of the normal expiratory phases and relative increase in the length of the so-called normal expiratory phase and distinct pauses are of frequent occurrence at the end of expiration. 4. Sudden changes from abnormal to costal, or from costal to abnormal, breathing occur frequently, both being observed at times in a single respiratory excursion, giving one the impression for the moment of a combination—a mixture of abnormal and costal breathing—and the frequent impression of inco-ordination—a dissociation in the respiratory movements. When 'pure abdominal breathing' occurs in chorea, movements of the whole chest are reduced to a minimum, and when 'pure costal breathing' occurs the upper abdomen remains practically motionless. 5. The respiratory rate is frequently accelerated and occasionally this may be slower than normal." These phenomena may be seen not only in the mildest cases, but may be also noted by palpation and auscultation, and some of them are among the earliest manifestations of the disease, continue prominently during its active

stage and are still perceptible after the other usually recognized motor symptoms have disappeared. This indicates not only that actual recovery may be long delayed, but that the recurrences often observed are true relapses. W. W. Graves (Jour. Amer. Med. Assoc., Jan. 30, 1909).

Deglutition in severe cases may be interfered with, and the patient naturally finds difficulty in feeding himself, on account of the inco-ordinate action of the muscles of the arms and hands. The urine and feces may pass involuntarily. The gait is, in all well-marked cases, altered, and is usually shuffling and slow, the steps being unequal in length and in time, with difficulty in progressing in a straight line.

There is no rigidity nor tonic spasm. The muscles may become tender to pressure. There is usually some muscular weakness or paresis, which, in occasional cases, becomes extreme ("paralytic chorea"). The tendon-reflexes are normal.

Some degree of muscular weakness can be detected in nearly every case of chorea. As a rule, the weakness is most obvious in the limb that is affected by choreic movements; thus, if this is the left arm it will usually be found that the grip of the left hand is weaker than that of the right hand, and that flexion and extension of the left wrist and the left elbow offer less force to passive resistance than the same movements of the right arm; weakness of the shoulder movements is less manifest.

Regarding the hand grip an apparent fallacy should be noticed; in some cases the movement of grasping is abnormally rapid and for a few seconds its strength seems to be excessive. These peculiarities may be due to a sudden choreic spasm, for the strength is only momentary, and cannot be maintained, the subsequent portion of the grip being distinctly weak, although it is to be noted that

the duration of the movement may be unusually long, the patient finding it difficult to relax the muscles. J. S. Bury (*Med. Chronicle*, Dec., 1909).

The writers practised lumbar puncture 20 times in 19 cases. The cerebrospinal fluid was perfectly clear in every instance. The pressure was apparently slightly increased in 1 instance. It had no noticeable effect on the symptoms. Morse and Floyd (*Amer. Jour. of Dis. of Children*, July, 1916).

Trophic disorders are not the rule, but erythema, herpes zoster, or chloasmic blotches may be occasionally seen.

There is always some disorder, usually a general dulling of tactile temperature and muscular sense. In the early stages pain is frequent, but in later stages this gives place to well-marked analgesia. Pricking, formication, and other paresthesiæ are common.

In uncomplicated cases the pupillary reactions are normal. Hippus is often observed in severe cases.

Case of chorea associated with embolism of the central artery of the retina. The patient was a young girl apparently in perfect health except for slight choreic movements of the right side.

There was no family history or past personal history of importance. The girl had never suffered from rheumatism. The unsteadiness of the right hand was noticed about six weeks before she first attended the hospital. There was a slight awkwardness in speech. She states that her left eye became suddenly blind when the trouble began, but the history is not definite. On examination of the heart a rough, blowing systolic murmur was heard at the apex. The left eye had no perception of light. The vision of the right eye was normal in all respects. The left fundus showed the ordinary appearances of embolism.

The case is of interest both from

the point of view of the ophthalmologist and from that of the general practitioner. H. Thomas (*Johns Hopkins Hosp. Bull.*, Oct., 1901).

Attention is called by the writer to the following symptomatic manifestations of the disease: (1) Hippus.—In many children who are more than slightly affected by the ordinary sthenic type of chorea the movements of the iris are extraordinarily wide and rapid. This is readily explained by the jerky movements of the eyeballs and the consequent quick and frequent variations in the amount of light which reaches the retina, and also the suddenly altering accommodation for the many objects which in turn are included in the visual field. This necessarily renders the detection of rhythmical oscillatory movements of the iris no easy matter, but during intervals of quiet these movements, which constitute hippus, are sometimes noticeable. (2) Peculiarities of movement of accommodation.—That the contraction of the pupils to accommodation may be extremely rapid and sudden has already been mentioned, but it will frequently be seen also that the reaction is asynchronous on the two sides, one pupil contracting, while the other remains temporarily dilated. This is especially marked when the pupils are unequal, the larger usually reacting more slowly. (3) Contraction.—Contraction of the pupils both to accommodation and to light is usually ill sustained, and here again the affection may be unequal, so that when both are contracted one will sometimes be seen, as it were, to tire out and dilate while the other remains small. (4) Varying inequality of the pupils.—It may be noticed in some cases that one pupil remains persistently smaller than the other during the complete examination. This may continue for several weeks and only be replaced by the normal equality when the child has recovered, or, on the other hand, when next seen the pupils may be equal or that which was formerly the larger

may now be the smaller. (5) Eccentric pupils.—Eccentricity of the pupils may occasionally be present and may become better marked when the pupil is contracted and less obvious when dilated. F. Langmead (*Lancet*, Jan. 13, 1908).

Psychical abnormalities are the rule. These vary from the slight irritability, weakness, and altered disposition commonly seen in early stages to marked intellectual impairment with loss of memory, confusion of ideas, inability to concentrate attention, and grave emotional disorder of a melancholic cast. Occasionally a generalized outburst of acute insanity or delirium will occur, giving rise to the clinical subdivision "chorea insaniens."

Case of that rare and terrible disease known as maniacal chorea or chorea insaniens. It is a form of chorea in which mania supervenes and completely overshadows the motor disturbances. So wide is the difference in the symptoms that it is hard to realize that it is not really another and a new disease, but only an exaggerated variety of the chorea simplex of Sydenham. The patient was an unmarried woman aged 17 years, and the prominent features of the case were: Rheumatic pains in the legs for a fortnight, upon which chorea supervened. A mitral systolic murmur, lasting up to the ninth day, the day of death. The pulse quiet and regular up to the last three days, when it rose to 120 to 140. The temperature normal until the day before death, when it touched 103.5° F. (39.7° C.). The choreic movements were slight for the first two days, after which they became so violent that two nurses were required night and day to prevent the patient falling out of the bed. The psychical phenomena were prominent out of all proportion, and at first quite overshadowed the motorial. They differed, however, by the absence of incoherent speech and wild garrulity

from the forms one is accustomed to associate with the acute delirium of fever or acute mania. Occasional, though temporary, mental calm occurred once or twice a day, up to the last three days. Treatment by medicines totally failed to have any effect, the only help it gave being by securing some hours of sleep and muscular rest. Finney (*Brit. Med. Jour.*, April 27, 1907).

The ordinary Sydenham's chorea, the acute chorea of childhood, may present mental symptoms which are very similar to those seen in acute infectious diseases. Almost all cases show increased irritability, peevishness, fretfulness, some loss of the power of attention, and selfishness. A second group shows night terrors and transient hallucinations. A third group shows delirium, which is usually accompanied by fever, and in a fourth group there is stupor and acute dementia.

The patients in the first two groups almost always recover mentally and physically; those of the third group frequently die, and those of the fourth usually either die or, recovering from chorea, remain demented. Burr (*Jour. Nerv. and Ment. Dis.*, June, 1908).

Acute chorea is distinctly a brain disease, and it is commonly characterized by both mental and physical, or motor, symptoms. The generally accepted classification of the mental symptoms is that of (a) mild mental symptoms, and (b) the psychoses. The first group represents much the larger number, and is characterized by symptoms involving chiefly the emotional field. In the second group delirious states leading to stuporous or paranoid conditions predominate. Diefendorf (*Jour. Nerv. and Mental Dis.*, March, 1912).

A true aphasia has been noted in a few instances, usually associated with a right hemichorea.

Along with the nervous symptoms above described in detail there are, in

most cases, some evidences of disorder of the general bodily functions. Fever is present at some stage, usually early, in a majority of cases. In maniacal chorea a temperature of 103° to 104° F. is often noted. A decided rise is usual in cases showing complications, such as rheumatism, pericarditis, or endocarditis.

The renal function is, in mild uncomplicated cases, normal. In the severe cases and in almost all febrile cases albuminuria exists, and the amount of urea excreted is in excess of the normal. In maniacal chorea there is, as a rule, a distinct nephritis.

The urine in Sydenham's chorea presents the following characteristics: diminution of the daily quantity; specific gravity relatively high; total acidity increased; diminution during the disease of the quantity of nitrogen which is not eliminated as urea; increased elimination of uric acid; decrease in elimination of chlorides; increase of phosphates; total quantity of sulphuric acid and allied substances unchanged. De Marchis (*La Riforma Medica*, July 5, 1902).

Cardiac irregularity with abnormal rapidity of action is not infrequent, and, of all the complications of chorea, pericarditis and endocarditis are most often seen, the latter, especially, occurring, according to Osler, in quite one-half of all cases. Cardiac murmurs, due to the endocarditis and also in some instances to impoverished blood, are common.

From a study and analysis of 108 cases of chorea treated at the Johns Hopkins Hospital and Dispensary, the writer concludes that there is good reason to think that well-marked febrile symptoms, without rheumatism, occurring in chorea, especially if they are accompanied with undue rapidity on irregularity of the pulse, is at least strongly suggestive evidence of acute endocar-

ditis. It is possible that the fever may be the sign of a deeper-lying infection back of the chorea, but there is nothing in his study to settle the question whether chorea represents a secondary infection or a special localization of an infectious agent responsible for essential manifestations of the disease. The study of the circulatory conditions in old patients still remains to be carried out, but the writer calls attention to the following points of interest thus far developed in his investigations: Of 689 cases of chorea observed at the Johns Hopkins Hospital and Dispensary one or more attacks, 25.4 per cent., showed evidences of cardiac involvement; such evidence was present in over 50 per cent. of the patients studied in the wards of the hospital. Cardiac involvement occurred with somewhat greater frequency in those cases in which there was a history of acute polyarthritis than where such history was absent, and was commoner in cases of chorea with frequent recurrences than in those in which there was a history of a single attack. In 110 cases of chorea treated in the wards of the hospital there was fever of a moderate extent in almost every instance. W. S. Thayer (*Jour. Amer. Med. Assoc.*, Oct. 27, 1906).

A true anemia—diminution in hemoglobin percentage and in number of red and white corpuscles—is often noted.

The blood of 40 children was examined for eosinophiles. The highest count was 26 per cent., the lowest 0, with a general average of 7.6 per cent. The possible relationship between eosinophilia and chorea is suggested. Berger (*Amer. Jour. Dis. of Child.*, May, 1921).

In a limited number of cases symptoms of gastrointestinal disorder occur, the symptoms being those shown in cases of autoinfection.

Three cases in which there existed a tendency to spasms and contraction of the gastric musculature and

sphincters, this motor restlessness entailing symptoms which proved rebellious to all ordinary methods of treatment. Skiagrams of the same stomach taken at a few moments' interval showed the remarkable changes in the shadow as the stomach curves up on itself, straightens out, or undulates in waves. The first patient had been treated for ten years without benefit, his frequently recurring attacks of gastric pain, vomiting, and exhaustion of the stomach having been diagnosed as gall-stone trouble, gastric crises, etc. But he was soon speedily cured by treatment directed to resting and counteracting the irritability of the stomach: **bed rest** for four to eight days, with **moist heat to the stomach**, no food beyond a small cup of milk every three hours from 7 A.M. to 7 P.M. for three to five days, then avoiding meat, bread, and all indigestible food for two weeks, interposing one "milk day" every four days. These measures were supplemented every two hours during the first week by a dessertspoonful of a mixture of 5 parts **bismuth** and 15 parts **acacia** in 150 parts distilled water. This patient was also given 3 Gm. (45 grains) of **sodium bromide** a day to act more directly still on the hyperesthesia of the gastric mucosa. The two other cases treated in the same way likewise recovered. Leven and Barret (*Presse méd.*, July 2, 1910).

Since chorea occurs by preference in children of neurotic heredity, the psychological, physiological, and anatomical stigmata of degeneracy in greater or less prominence are often added to the symptoms above detailed.

Three grades of the disease are described: The mild, in which there is little disturbance of general health, no complications, and only moderately well marked choreic movements; the severe, in which fever, mental disorder, and other complications are present, and the inco-ordinate clonic spasms more severe

and continuous, with well-pronounced muscular weakness; and the violent "chorea insaniens," characterized by rapid onset and progress, violent and continuous choreoid spasm, with fever and delirium, terminating not infrequently in death.

Fatal case of chorea in a child 10½ years of age. It is very infrequent for a child over 2 years of age to die of chorea. The patient had an attack of acute mania with hallucinations in the course of his illness. The autopsy did not show the usual lesions of chorea, the thymus only being found enlarged. Sepsis is supposed to have been the cause of death, streptococci having been found in the blood, which probably entered through abrasions in the skin or the mucous membranes. This fact emphasizes the need of caution in keeping wounds of the skin or mucous membranes in these little patients scrupulously free from contamination. J. Hallé and G. Langevin (*Archives de méd. des enfants*, Aug., 1900).

**DIAGNOSIS.**—In typical cases no great difficulties in diagnosis are presented, the characteristic muscular movements being, in themselves, sufficient to make the nature of the case plain. In atypical forms some doubt may arise, and there are a few other states which may be confounded with acute chorea. Thus, in hysteria choreiform movements suggesting chorea may take place ("hysterical chorea"). The anesthesia and accompanying symptoms discoverable upon examination, together with the fact that in hysteria the movements are more rhythmical than in chorea, should make a diagnosis easy.

The muscular weakness may be so extreme as to suggest acute anterior poliomyelitis. The presence of the choreic movements is, however, enough to exclude poliomyelitis. Some forms

of sclerosis and degenerative changes in the cerebral cortex are attended by choreiform movements, and may, when occurring in young persons, lead to thought of acute chorea. The presence of mental disorder, exaggerated reflexes, muscular rigidity, and other spastic symptoms should prevent mistake. Friedreich's ataxia was formerly and is still sometimes mistaken for chorea by those unfamiliar with the symptomatology of nervous diseases. The scanning speech, nystagmus, and the irregular, slow, and peculiar inco-ordinate movements of Friedreich's ataxia are sufficiently different from the clinical picture of chorea to prevent confusion if a proper examination is made.

One cannot rely on the movements alone for a diagnosis of chorea; some children subject to choreic attacks never have the typical choreic movements, or the movements may occur in one attack and be absent in another. There are also cases in which the movements are tic-like from the beginning, and others in which typical attacks of chorea pass, as it were, into conditions of tic. The distinction between tic and choreic movements is an important one. The tic is an affair of a higher cerebral level, so to speak; it is closely related to psychic functions, while the choreic movement, on the other hand, is due to some defect in the motor inhibitory apparatus, a simpler cerebral function. I R. Fry (Jour. Amer. Med. Assoc., May 2, 1908).

Characteristics, respectively, of chorea and motor tic, or what is known sometimes as habit spasms. The movements of chorea are involuntary and scarcely at all under the control of the patient. Those of tic, however bad, are always volitional even if not voluntary. There is never in chorea the complete control which can always in some way or other be shown to exist in tic. In chorea, the movements are inco-ordinate and

purposeless and such as a well person never makes. On the other hand, the movements of tic are co-ordinated and repeated over and over again. When choreic movements grow worse and spread, they do so without relation to anatomical or physiological groupings, except that in the beginning and in mild cases they are apt to be limited to one side of the body. A tic extends in one of two ways, ordinarily by involving adjacent and functionally related groups of muscles. Or it may spread by starting a really new tic in another part of the body in a susceptible person. Chorea is notoriously disabling, and one of the earliest signs is the unexpected dropping of things. Tic, on the other hand, is troublesome, but scarcely disabling. The patient with tic of the arm writes as well as ever; his arm does not jerk his hand unawares. Another striking difference is that the movements of chorea are physically distressing and uncontrollable, while those of tic give a certain relief. A man who has suppressed his tic feels more comfortable when he is over the suppression and can go on a little spree of tics. While convulsive tic is almost purely motor in its manifestations and its inception, the writer thinks that its origin is almost always sensory. Some cases seem to start as a mere nervous fidgetiness, a vague sensation of discomfort which finally develops into a tic. Sometimes the disorder seems to rise from imitation, and this is also sensory, but what he specially wishes to insist on is that tic is never a "reflex neurosis." He makes a comparison between tic and spasmodic torticollis, which is clearly not a local disease, an affection of the spinal accessory nerve or of the neck muscles. The points of resemblance he mentions are as follows: "1. The subject of a spasmodic torticollis, as the subject of tic, is always a neuropath. He shows the same sort of abnormal susceptibility, the same psychomotor inability, the same lack of inhibition.

Several times he thought he had found an exception to this rule, but in each case more intrinsic acquaintance with the patient showed the error of his first impression. 2. What has been said of the sensory origin of the tic applies to spasmodic torticollis. For example, muscular rheumatism, the ordinary 'stiff neck,' is not rarely the origin of the trouble. 3. The emotional state of the patient has much to do with the neck spasm. It is always worse when the patient is self-conscious or 'upset.' On the other hand, intense mental preoccupation may entirely abolish the trouble for a brief space. 4. In torticollis there is the same strain in repressing the muscular drawings as in the other tics, and the same sense of relief in 'letting it go.' A patient riding in a street car will repress the movements until he can stand it no longer, then he will hide behind his newspaper and have a little motor indulgence, which gives him a measure of sensory satisfaction or relief. 5. The muscular contractions of spasmodic torticollis are not true spasms; they are volitional. And they always are more or less under voluntary control. . . . 6. The patient with spasmodic torticollis invariably has some trick of restraint: what Brissaud has called a restraining gesture. It is one of the most striking things connected with this neurosis. A man whose neck muscles are twisting his head around with the greatest violence will gently place a finger against his chin or lay his palm over the occiput, when the muscles at once relax and the head assumes its normal position. H. T. Patrick (*Jour. Amer. Med. Assoc.*, May 1, 1909).

**ETIOLOGY AND PATHOLOGY.**—In general terms, choreic movements of all kinds are primarily due to inherent neuronc weakness or instability, especially in motor sphere, with abnormally developed motor association tracts, or to defective insulation in lines of motor discharge.

The immediate exciting cause is irritation of cortical motor neurons from toxic substances in the blood due to infectious diseases, autointoxications, etc., nerve-cell fatigue, and in some cases temporarily induced abnormal "neuronic contacts" in sensorimotor sphere from sudden shock or emotion.

The clinical sequence of tonsillitis, articular rheumatism, with chorea or endocarditis, points to a localized lesion producing periodic systemic infection. Experimental work showed a much higher percentage of carriers of certain types of virulent streptococci in the substance of the tonsils and about the teeth in cases of chorea than occur in normal controls. He concludes that the teeth and tonsils, in all probability, offer 2 portals of entry to the body for streptococci in producing any one of these clinically grouped diseases. Floyd (*Jour. Med. Research*, May, 1920).

In the form of acute chorea under consideration the neurotic constitution with the anatomical and physiological stigma of degeneration can usually be traced. Anemia with general bodily enfeeblement is common.

Some cases develop without any discoverable exciting cause, but in most instances the onset of the chorea is preceded by mental strain, worry, or shock of some kind—overwork at school, fear, religious emotion, etc.—or by the occurrence of some infectious disease or toxemic state, such as rheumatism.

Measles, whooping-cough, influenza, diphtheria, scarlet fever, endocarditis, malaria, urinary abnormalities, aggravated constipation, etc., are also important factors.

Rheumatism was formerly deemed an important etiological factor of chorea, the cardiac lesions being closely associated with it. Both the rheumatic diathesis and cardiac morbid conditions predispose to the disease.



More recent studies indicate that a variety of bacterial toxins and auto-genic poisons are potent etiological factors.

The effects of the pathogenic toxic are much more widely spread over the body than on articular or cardiac structures, and the throat and skin, or the brain, may equally be sites for the manifestations. The pathology of choreic endocarditis is identical with that of rheumatic endocarditis. Rheumatism has been clearly proved to be an infective malady, and the specific causative organism has probably been identified—the diplococcus of rheumatism of Poynton and Paine, the micrococcus of Walker, and the streptococcus of chorea of Wassermann, being all three identical. Although chorea is never caused by nervous shock or fright, yet a neurotic factor must be acknowledged in a true conception of its pathogeny. That the young and the female sex afford the greater number of examples of it is probably due to the fact that in these subjects the rheumatic toxin is apt to spread more widely and to act with greater intensity than in adults. The adolescent brain is also more unstable than the fully developed one. Chorea is distinctly more frequently met with in families prone to rheumatism; it may precede by months or years an attack of rheumatic fever or may supervene during an attack. The disease occurs markedly among the nervous or unstable members of a family. It is thus a true cerebral rheumatism. It is certain that there is something specific in the nature of the rheumatic toxin as introduced by the particular infecting microbe. It is probable that the toxin varies in the quality and degree of its virulence. Sir Dyce Duckworth (*Brit. Med. Jour.*, June 23, 1906).

There is less real association between chorea and rheumatism than is generally thought to be the case. Chorea may be due to an infective toxemia of distinctive character. The

writer's experiments show (1) that there appears to be in the blood-plasma of patients suffering from chorea a poison which is toxic to the leucocytes of healthy persons, and (2) that in rheumatism the plasma does not appear to be so uniformly toxic; in fact, it seemed to be hardly at all poisonous to healthy leucocytes. In the first 2 cases of chorea which were investigated there was a marked eosinophilia. The counts showed 20 per cent. of eosinophiles in one, and 16 per cent. in the other. This might possibly have been due to some unsuspected intestinal parasites, but examination of the stools for eggs, etc., gave absolutely negative results. Macalister (*Brit. Med. Jour.*, Aug. 28, 1909).

An analysis of 300 cases by the writer showed that 53 per cent. had definite signs of rheumatism either previously to or concurrent with the chorea; 72 per cent. showed a personal or strong family history of rheumatism. In a large number there was a history of nervous diseases in other members of the family. In comparing the age incidence, Fraser, agreeing with Guthrie's figures, found a marked increase in chorea between 6 and 12 years, and in acute rheumatism between 7 and 12 years. The seasonal incidence, agreeing with Gabbet, showed the maximum of chorea one month later than rheumatism. According to the observations of Batten, 25 per cent. of 115 chorea patients treated at the time, without signs of rheumatism, developed it within six years. M. S. Fraser (*Pract.*, March, 1912).

An exhaustive histologic study of a case of chronic progressive chorea showed that the involuntary movements were probably due to a primary degeneration of the neurons in the nucleus ruber, the lateral nucleus of the optic thalamus and the lenticulate nucleus, thus interfering with the conductive integrity of the cerebello-thalamo-rubro-cortical path. The brain and spinal cord, including the motor cells were well preserved.

Pfeiffer (*Amer. Jour. of Insanity*, Jan., 1915).

Chorea is of infectious origin. In 143 of the hospital cases in which a special history of rheumatism was mentioned only 13 gave a definite history of articular rheumatism. The findings were similar regarding chorea and tonsillitis; only 45, or 33½ per cent., gave a history of tonsillitis. These records did not justify the assumption that there was any relation between chorea and acute infectious diseases. There was no question but that shock might bring on the symptoms of the disease. Of 226 cases, 73 showed cardiac affections, the majority being diagnosed as mitral. Isaac Abt (*Med. Rec.*, June 24, 1916).

Experience with 211 cases of chorea suggested that it is a neurosis which develops in the predisposed mainly between the 8th and 12th years in boys, and 2 or 3 times as often in girls; usually between the 6th and 14th years in girls. The exciting causes may be of infectious or toxic nature or emotional stress, but the predisposed age is the period of most active growth. The years closest to puberty are less affected. Out of 217 cases of pregnancy chorea in 140 developed in the first half of the pregnancy. Out of 224 cases of pregnancy chorea, 106 were under 21 and 102 between 21 and 26, leaving only 16 older than this in the total 224 cases. Youth in the pregnant women is thus a predisposing factor to pregnancy chorea. Infections, autointoxications and emotional stress may be the source of the reflected irritation in the pregnant as well as in children. C. Schiotz (*Norsk Mag. f. Laegevid.*, Apr., 1917).

In a study of the bacteriology of chorea the writer made cultures from the tonsils, the blood and cerebrospinal fluid of acute, subacute and chronic cases of chorea. Blood cultures were made in 21 patients, 10 of whom gave positive results; 9 gave small cocci, slightly elongated and arranged in pairs, short chains, and

a few groups, in aerobic cultures, 1 gave a Gram-positive short diphtheroid organism. The cerebrospinal fluid of 21 patients has been cultured, with 13 positive results. Of the 21 patients 11 gave histories of acute tonsillitis, 2 of rheumatism, 1 of endocarditis, 8 gave no history of rheumatism, endocarditis, or tonsillitis. None gave any evidence of syphilis. Quigley (*Jour. of Infect. Dis.*, Mar., 1918).

The frequency of fibrinous accretions upon the cardiac valves and the undisputed frequency of embolism of the cerebral arteries give origin to the often-mentioned "embolic theory" of the causation of chorea, a theory first advanced by Kirkes and supported especially by Hughlings-Jackson, according to which the inco-ordinate movements of chorea are due to multiple capillary embolism of the corpus striatum. This explanation is, however, somewhat far-fetched, and it is also insufficient, since there are many cases of chorea which show no evidence of embolism and in which there is no endocarditis.

A specific microbic origin has been suggested, but, while the diplococcus of rheumatism of Poynton and Paine affords promise in this direction, its specific nature has not as yet been demonstrated.

Two cases of chorea in which the cause was a severe general infection. Its possible infectious nature has been spoken of for the last thirty-five years, and in a number of instances micro-organisms have been isolated from the blood and tissues of individuals whose death ensued in the course of chorea; in but few, however, have septic organisms been isolated from the blood of the living subject suffering from the chronic disorder. In the first case blood examinations made during life demonstrated staphylococci; in the second case no organisms could be isolated. The writer suggests the following

Should any indication of chorea appear, the child should be removed from school at once and placed in as good hygienic circumstances as possible. The child's attention should not be directed toward the disease, and the nervous manifestations should not be openly noticed nor commented upon by others, since self-consciousness and suggestion play an important part in exaggerating the choreic symptoms. Removal of the patient from home, relatives, and familiar surroundings will go far toward relieving the condition. A trip to the country or to the seashore when possible is always beneficial. **Massage and hydrotherapeutic measures** are almost always indicated, and do especial good in the cases in which anemia and general debility are present.

Any degree of **focal infection** may cause or aggravate through the resulting toxemia all the clinical phenomena of the disease. The tonsils, teeth, gastrointestinal canal, the sinuses, etc., should be carefully examined and any local disorder should be **eradicated**.

In severe cases **rest in bed** for a few days or even for weeks is advisable, and in the severest cases is made necessary by the violence of the contortions, which may entirely prevent the child from walking or standing. With these non-medicinal restorative measures the patient will usually recover within a month or two, but in most cases there can be little doubt that restoration is hastened by proper medicinal treatment.

The main factor in treatment is a tranquilizing environment, with care for nourishment and sleep, with nothing read or told the patient to excite him. Prolonged **warm baths** are often of decided benefit, keeping the water constantly at 34° to 37° C.

(93.2° to 98.6° F.). Three such baths can be given during the day; the appetite and need for sleep are much promoted thereby, but anything in the way of a pack irritates and frightens a child with chorea. J. Grober (Deut. med. Woch., May 2, 1912).

The drugs which experience has shown to be most useful are arsenic, strychnine, the **zinc salts**, **silver nitrate**, **potassium iodide**, and **cimicifuga**, the latter in 30-minim (2 Gm.) doses three times daily.

In view of the prevailing belief that chorea is a clinical manifestation of a hidden infective process, the writer injects directly into a convenient vein 10 minims (0.6 c.c.) of a 1 per cent. solution of **carbolic acid**. This is usually done on 3 successive days. In some instances 1 injection caused a remarkable improvement, while in others over 3 injections were given, a period being allowed to elapse between the third and subsequent ones. Mayer (Intern. Clinics, vol. 1, p. 1, 1916).

Of all these **arsenic** in gradually increased doses until its physiological effects appear is preferred by most clinicians.

According to William Murray, the first or "one of the first" to recommend arsenic in this disease was Thomas Martin, of Reigate, England, in 1813. The case successfully treated was a severe one judging from the symptoms recited.

Study of 1400 cases of chorea. **Arsenic**, pushed to the physiological limit, and then reduced slightly, is the best drug in the treatment, and antipyrin is second; exalgin, phenacetin, bromide, chloral, and paraldehyde produced little effect. Better than any medicine is a **change of air**. M. Allen Starr ("Jacobi Festschrift"; Phila. Med. Jour., May 26, 1900).

The writer has found by experience that as soon as the dose is increased

beyond 12½ minims (0.75 c.c.) there is danger of the **arsenic** being rejected. His contention is, then, that it is possible to rapidly saturate the tissues, and so stop the choreic movements, without producing the symptoms of acute poisoning, and by doses very much smaller than those usually prescribed and considered necessary to relieve the chorea. In a case of chorea of from 8 to 15 years of age, and between these ages one oftenest meets with the affection, he prescribes the following:—

**R** *Arsenical solution* (Fowler's) ..... ℥ccxl (or sometimes ccc) (15 c.c.).  
*Tincture of capsicum* ..... ℥xxv (1.55 c.c.).  
*Liquid extract of licorice* .. ℥ccxl (15 c.c.).  
*Chloroform water* ..... f℥vj (180 c.c.).  
*Water* to make f℥xij (360 c.c.).

Mix. Take 1 tablespoonful three times a day immediately after meals.

The quantity in the foregoing prescription is for eight days, or, roughly, a week, and this is useful in out-patient practice, for no case of chorea should be left unseen for a longer period than one week. In private practice it is better, perhaps, to prescribe only half the quantity, namely, 6 ounces (180 c.c.). J. Gordon Sharp (Pract., Jan., 1908).

Histories of children having chorea who were treated successfully with the solution of **arsenous acid**, 1:1000, used by Comby. This solution is much better borne than Fowler's solution and is effective much more quickly, some cases seeming cured after two to three days of treatment. Each teaspoonful of the solution contains 4 mg. ( $\frac{1}{10}$  grain) of arsenic. This is given in large doses well diluted, increasing for seven days, and then decreasing. The authors, in their 4 reported cases, used smaller doses than Comby, of the same solution. Their conclusion is that in

these doses it is safer than Fowler's solution, improvement sets in more quickly, the duration of the disease is shortened, and the by-effects of arsenic can be avoided or mitigated.

G. B. Hassin and A. M. Hershfield (Med. Rec., July 2, 1910).

**Arsenic** is believed by some authors to prove less toxic when administered with butter.

Experiments performed in 1879 by Chapuis have shown that **arsenic** when **combined with butter** appears infinitely less toxic than when given in solution. These investigations, personally repeated, show that the amount of butter should be invariably fixed to 10 Gm. (2½ drams), whatever the quantity of active principle incorporated with it. To prepare the mixture a known quantity of arsenous acid is taken according to the dose to be administered. To this is added sodium chloride in such proportion that 0.1 Gm. (1½ grains) corresponds to 0.005 Gm. ( $\frac{1}{20}$  grain) of arsenous acid. This mixture of sodium chloride and arsenic is triturated with 10 Gm. (2½ drams) of fresh butter, and this amount is given spread on bread: a form of medication which is extremely palatable to children. The drug must never be administered while fasting. The whole dose should be given at a time, but two doses a day seem to be sufficient. Under this method of treatment it is not necessary to confine the patient to bed or to put him on a milk diet. A more liberal diet gives better results. Lévy (Thèse de Lyon, 1900).

In view of the experiments of Chapuis, who had observed that arsenic incorporated in fats produced little or no toxic effect in animals, the writer adopted the plan of administering arsenic trioxide to choreic patients in the form of "**arsenical butter**." In the preparation of this he takes approximately that amount of arsenic which will be required during the entire course of the affection, say, 0.18 Gm. (2½ grains), and adds to it 3.6 Gm. (55 grains) of sodium chlo-

ride or milk-sugar. A mixture is thus obtained which is more easily weighed out than the arsenic alone, and each 0.1 Gm. ( $\frac{1}{2}$  grain) of which contains about 0.005 Gm. ( $\frac{1}{12}$  grain) of arsenic trioxide. Of it he administers on the first day 0.1 Gm. ( $1\frac{1}{2}$  grains); on the second, 0.2 Gm. (3 grains); then 0.3, 0.4, and 0.5 Gm. (5,  $6\frac{1}{2}$ , and 8 grains), after which the dose is gradually reduced again. Each dose is given triturated in 10 Gm. ( $2\frac{1}{2}$  drams) of butter, which is spread on bread and taken with the principal meal of the day. The effects obtained by administering arsenic trioxide in this way are the same as when it is given otherwise, but toxic effects are entirely avoided. Rest in bed and milk diet, moreover, are quite unnecessary with it. Sodium arsenate or potassium arsenite should not be substituted for the trioxide in the arsenical butter, as the latter is then not so well borne. E. Weill (*Progrès méd.*, Jan. 6, 1912).

The use of arsenic is contraindicated when renal or cardiac lesions are present; in advanced cases attended by paralyses; during active rheumatic manifestations, especially when neuritis is present.

Several cases of neuritis which supervened after the cure of chorea by **arsenic**. In these cases 10 drops (0.6 c.c.) of liquor arsenicalis had been given thrice daily for three or four weeks, by which time the patients had taken an equivalent of from 6 to 8 grains (0.4 to 0.5 Gm.) of arsenous acid. None of the cases gave any warning of the advent of the neuritis during the administration of the arsenic, but the symptoms developed after an interval of from a week to a fortnight subsequent to its discontinuance. No dose amounting in the aggregate to more than 4 grains (0.26 Gm.) of arsenous acid should be administered to a child suffering from an attack of chorea. Railton (*Med. Chron.*, Feb., 1900).

The treatment of *chorea* with **arsenic** is inadvisable:—

1. In very acute cases with coma or paralysis.

2. In those that have been treated for some time with small doses of arsenic.

3. In those in which there is reason to suppose that the rheumatic process is going on in the acute form.

4. In cases of advanced cardiac disease.

The writer gives the following principles for the administration of arsenic in the treatment of chorea: 1. See that the tongue is clear before commencing treatment, and, if not, give a mild mercurial purge and a stomachic mixture for forty-eight hours. 2. Put the patient on a bland and easily digested diet. 3. Give the drug in a much diluted form and in the same dilution throughout. 4. Do not discontinue on the first attack of vomiting, which may be due to accidental causes. 5. Increase the dose daily. 6. Keep the patient in bed throughout the treatment. 7. If the vomiting persists, discontinue the drug for twenty-four hours and then give the same dose as the last. 8. Examine the patient very carefully daily for any sign of toxic action. What must be aimed at is a form of shock action on the nerve tissues, and this may explain why long-continued treatment with small doses fails. On discontinuing the arsenic, the writer usually gives a mixture containing iron for a few days. Pope (*Brit. Med. Jour.*, Oct. 18, 1902).

The writer discourages the use of Fowler's solution of arsenic in chorea as producing nephritic symptoms, such as albumin and casts, before the swelling of the eyes occurs. When this drug is given it should be accompanied by very careful examination of the urine daily, and its use should stop as soon as any signs of nephritis are shown in the urine. Most cases are better treated without it. Neuritic symptoms are sometimes caused by it that make the pa-

tient's condition worse. The best treatment is a **modified rest cure**. Isolating a child in bed in a dark room is not only unnecessary but injurious. The child becomes restless and depressed, instead of benefiting by it. The child should have additional rest and a full diet, but should be allowed some quiet play and companionship, with plenty of **fresh air and sunshine**. Hydrotherapeutics are of great value and liked by the child. Arsenic is especially dangerous in cases in which the heart is involved, and in cases of chorea in which there is loss of speech, paralytic symptoms, and mental depression. **Sedatives** and **strychnine** are the best remedies with **rest** and **hydrotherapeutics**. Henry Koplik (Med. Rec.; Jan. 18, 1908).

When arsenic is not well borne **sodium cacodylate** might prove useful.

Three cases cured by means of rectal injections of **sodium cacodylate**. The patients were girls of 12, 14, and 8 years respectively. A solution of 1:400 was employed, of which 1 injection of 5 c.c. (80 minims) was practised (in the first 2 cases) daily for five days, then 2 injections for the next five days, then 3 injections of a similar dose for the succeeding five days, after which the injections were suspended for five days, and then begun over again, as before. The total of sodium cacodylate taken during a month of treatment amounted to 0.75 Gm. (12 grains), and at the close of this period not the slightest sign of chorea was to be perceived; nor did any symptoms supervene even after two weeks' suspension of all treatment. The third case was similar, only the doses were smaller. Besides the very pronounced success, it is remarkable that not the slightest phenomenon of intolerance was exhibited by the patients. Garand (Les nouveaux rem., vol. xvi, p. 276, 1900).

Three cases of chorea treated with **sodium cacodylate** instead of arsenic. The former drug given hypoder-

mically, first in doses of  $\frac{1}{8}$  grain (0.022 Gm.), then of  $\frac{3}{8}$  grain (0.044 Gm.). The patients recovered in from one to three weeks. In all, ordinary treatments had been tried without benefit. Lannois (Revue de therap. méd.-chir., lxxviii, No. 5, 1901).

The addition of **strychnine** or of **ergot** to the arsenic has been deemed advantageous by some.

In children particularly **ergot** acts as a very valuable sedative, this action being due to its influence on the blood-supply, on the nerve tissues in the spinal cord in part, or perhaps a direct sedative. No ill effects were observed, although the writer gave doses of a dram (4 Gm.) every hour for three weeks for children 7 or 8 years of age and doses of 20 drops (1.25 c.c.) or more for many months at a stretch. In chorea its action is not as reliable as Fowler's solution, but often arsenic is not well borne by many patients. Ergot acts more quickly than arsenic. It is sometimes necessary to push the doses of the remedy, boys seemingly requiring larger doses than girls. Eustace Smith (Brit. Med. Jour., No. 2220, p. 133, 1903).

Effects of a combination of **ergot** and **arsenic** in 35 cases of chorea. The ergot was given in doses of 1 to  $1\frac{1}{2}$  drams (4 to 6 Gm.) of the liquid extract, three times a day, with 2 minims (0.12 c.c.) of liquor strychnine. [Liquor strychninæ of the British Pharmacopœia consists of 1 grain (0.065 Gm.) of strychnine sulphate to 110 minims (6.25 c.c.) of distilled water.] These doses did not give rise to symptoms of poisoning, nor to any appreciable physiological effects. About half of the patients were rapidly improved or cured by this means and most of the remainder improved when arsenic was substituted. That it is the drug treatment which was effectual in these cases is beyond question, because often when it was stopped a relapse occurred and the patient was

again cured or improved by its re-administration.

In 2 cases, the ergot treatment was ineffectual; arsenic made the patients worse, but on returning to ergot they were immediately improved. This experience suggested the advisability of trying ergot and arsenic in combination. The mixture used contained 1 dram (4 Gm.) of extract of ergot and 3 minims (0.18 c.c.) of Fowler's solution, these doses being increased as seemed desirable. There are few patients who remained unbenefited by this treatment; in the majority the improvement began at once. The unbenefited cases consist mainly of those violent choreas for which so little beyond isolation can be done. Riviere (*Brit. Med. Jour.*, Feb. 18, 1905).

**Chloretone** sometimes proves efficient in cases in which arsenic fails.

We may expect an attack of chorea of moderate severity to last six or eight weeks if treated by rest, and arsenic is administered; if arsenic fails, then the **zinc** compounds or **belladonna** may be tried. Dr. Essex Wynter, in the *Lancet* of March 30, 1907, records his results of treating 14 cases of chorea with chloretone, saying: "The choreic movements were limited to nine days, and the stay in hospital to three weeks on an average." The writer tried **chloretone** in 12 cases, all of which have been so treated, and the result has been uniformly good. The cases were consecutive ones and not picked; the ages of the patients varied from 5 to 15 years, and, with one exception, all were girls. The average duration of the choreic movements after beginning treatment by chloretone was eleven days; the length of their stay in hospital was not reduced, however, for I kept the patients in for some time to see if there would be any relapse. In 2 cases only was there any return of choreic movements; both were very bad cases, but in each the relapse was cured in three days and two days respectively

by putting the patients again on chloretone, and in neither case has there been any further return. J. George Taylor (*Folia Therapeutica*, Oct., 1908).

Case in which arsenic in the form of Fowler's solution was administered until the physiological limit was reached. The child failed to improve; the choreic movements were just the same as before treatment. The arsenic was stopped and in place of it the writer gave  $\frac{1}{2}$  grain (0.032 Gm.) of **chloretone** three times a day, increasing by  $\frac{1}{2}$  grain (0.032 Gm.) a day until 2 grains (0.13 Gm.) three times a day was reached, and then the dose was decreased by  $\frac{1}{2}$  grain (0.032 Gm.) a day until it was stopped altogether. After the first day a marked improvement was noticed. The child had a soft systolic murmur at the base, which was entirely gone at the end of treatment. Ten months after treatment she had not had a relapse. H. B. Orton (*N. Y. Med. Jour.*, Nov. 20, 1909).

As emphasized by von Bechterew, the administration of sedatives often aids arsenic materially in hastening the cure. **Antipyrin** or **trional** may be used for this purpose or alone.

Having had some unsatisfactory results with Fowler's solution, particularly in the case of a girl aged 9 years in which the choreic movements seemed to increase, which led to exhaustion from sleeplessness, the writer tried **trional** in 3-grain (0.2 Gm.) doses every four hours. Good results were manifested almost at once. The patient ultimately recovered.

The writer has tried the same drug in several other cases with equally happy results. **Trional** and **sulphonal** should be given in doses of 2 grains (0.12 Gm.) every four hours to a child of 10 years. The dose can be increased or diminished as the case may indicate. Adams (*Archives of Pediatrics*, May, 1899)

Satisfactory results from **antipyrin** given according to Eskridge's method. The drug is given in increasing doses, beginning with 1 grain (0.065 Gm.) for each year of the child's age, and increasing 1 grain (0.065 Gm.) each day. In the mildest cases the child is allowed to sit up a part of the day, and the antipyrin is only given in the evening, but in severe cases absolute rest in bed is necessary, the dose of antipyrin being given three times a day. The drug is stopped as soon as the choreic movements cease or greatly diminish. **Fowler's solution and iron** are given until two or three weeks after the cure appears to be complete. In giving such doses of antipyrin (20 grains—1.3 Gm.—three times a day to a child 8 years old) the child must be kept in bed and carefully watched; should there be heart disease or any fever, it is not given. Rapid cures were obtained in 19 cases so treated. S. D. Hopkins (Phila. Med. Jour., Aug. 19, 1899).

In addition to **absolute rest** in bed, a strict **milk diet**, and **hydrotherapy**, the writer recommends gradually increasing doses of **antipyrin**. In 40 cases this method cured the patients in from twenty to twenty-five days on the average. The administration of antipyrin should be carefully watched, and its use should be suspended in the event of albuminuria, marked weakness of the pulse, or other toxic manifestation. Langevin (Jour. de méd. de Paris, Jan. 1, 1906).

The writer recommends **trional**, the value of which in chorea has not been universally recognized. It is most efficient in controlling the movements, producing sleep, and effecting a rapid cure in the great majority of cases. S. F. A. Charles (Dublin Jour. Med. Sci., Nov., 1911).

**Hyoscine hydrobromate** has also been found of value in this connection.

Case of acute chorea in a boy 16 years old in which potassium bro-

midate, chloral, and arsenic failed to give relief. When admitted to the hospital he had constant and universal involuntary movements; the tongue was dry and brown, and was severely bitten; the temperature was somewhat elevated, the pulse was weak, and the respiration irregular. His condition soon became apparently hopeless. **Hyoscine hydrobromate**, in doses of  $\frac{1}{200}$  grain (0.0003 Gm.), was given hypodermically twice daily and was soon followed by improvement. The dose was increased to  $\frac{1}{100}$  grain (0.00065 Gm.) thrice daily, and within a week the movements had almost subsided. Subsequently **Fowler's solution** was used, and the patient made a complete recovery. The writer adds that chorea is rare in India, but usually fatal. Rendle (India Med. Rec., Aug. 30, 1899).

Case illustrating the rapid and satisfactory results from the administration of **hyoscine hydrobromate** hypodermically in doses of  $\frac{1}{200}$  grain (0.0003 Gm.),  $\frac{1}{150}$  grain (0.0004 Gm.),  $\frac{1}{100}$  grain (0.00065 Gm.), after bromides had proved unsatisfactory. In the discussion, Crozer Griffith said that the case had been under his care and no words could well describe the violence of the movements. It was interesting to watch the excessively irregular movements of the diaphragm, as well as the difficulty which the child experienced in taking any food. The case was also an illustration of the value of hyoscine in this condition. Isaac H. Jones (Archives of Pediatrics, Aug., 1908).

The quieting effects of **hydrobromate of hyoscine** in maniacal excitement led the writer to employ it in chorea. The first case was very severe, occurring in a man 18 years of age. The disease began without prodromata and developed very rapidly. Within the first three days the movements were so violent that the patient was confined to the bed and had to be placed between mattresses to prevent injury. The mus-



cles of the face were involved. The hydrobromate of hyoscine was given hypodermically, twice daily, and combined with 20 grains (1.3 Gm.) of **chloral** and a similar quantity of **ammonium bromide**. At the end of five days involuntary movements ceased. Hydrobromate of hyoscine has been given in 20 cases of more or less severity. In some of the cases it has been combined with **Fowler's solution**, but in others it has been given alone. It is given in doses of  $\frac{1}{200}$  to  $\frac{1}{60}$  grain (0.0003 to 0.0013 Gm.), according to the age and the severity of the attack. In some cases it was found that the hyoscine was ineffectual if given by the mouth, even in those in whom the digestive functions seemed to be normal. W. B. Ewing (Penna. Med. Jour., Nov., 1911).

It is always to be kept in mind that chorea is a symptom, in many instances, of some general bodily enfeeblement or disease; a thorough and searching physical examination should invariably be made.

The likelihood that rheumatism is the underlying cause of the choreic symptoms should always be borne in mind. The tonsils should be examined and treated by means of a solution of 1 part of **Lugol's solution** to 4 of glycerin applied locally to the follicles or crypts. Internally either the **potassium iodide** or **salicylates** should be used, giving preference to the latter if the pain is severe.

Every child who complains of sore throat or of pains in the joints, muscles, or tendinous structures, or who suffers from malaise and unexplained pyrexia, or whose skin shows spots of erythema or who has subcutaneous nodules on his tendons or round his joints, or subperiosteal nodules on his bones, or who has pain in the chest, or shortness of breath, or marked pallor, or who exhibits even slight choreic movements or merely weakness and inco-ordination of mus-

cular action or emotional instability, be at once put to bed, and his heart should be promptly and most carefully examined.

The writer cites Poynton and Paine's demonstration of a diplococcus in rheumatism and chorea which is capable of producing in rabbits not merely endocarditis, but cardiac dilatation, myocarditis, pericarditis, arthritis, pleurisy, and pneumonia, also subcutaneous nodules and tenosynovitis; in short, all the severe lesions found in a rheumatic child. He adds two facts within his own knowledge: (1) a rheumatic nodule excised from a child, which gave on culture an exuberant and pure growth of a diplococcus; (2) the obtaining of a diplococcus from the blood in more than one case from rheumatic patients during life. With regard to chorea, although it has not yet been proved that chorea in a child is in all cases of rheumatic origin, yet it is quite certain that the great majority of cases are due to a rheumatic infection. Every case of chorea in childhood ought, therefore, to be considered as presumably rheumatic, and ought to have the benefit of this probability. Every such patient ought to be at once sent to bed, and treated vigorously as for rheumatism. D. B. Lees (Brit. Jour. of Children's Dis., March, 1909).

Of 780 hospital patients studied, 355 were given **salicylates** and 425 received other treatment: 156 received doses of the former below 60 grains (4 Gm.) a day, 95 between 60 and 100 grains (4 and 6.65 Gm.), 60 between 100 and 200 grains (6.65 and 13.3 Gm.), 19 between 200 and 300 grains (13.3 and 20 Gm.), and 8 received doses of more than 300 grains (20 Gm.) a day; the remaining patients were treated with **acetosalicylic acid**. If the drug has no effect the numbers showing cardiac change should be in the proportion of 39 untreated to 32 treated with salicylates, and the actual numbers obtained are so near these that the disparity can have no significance. It might be thought that the larger

doses would have had more effect in preventing the progress of the cardiac trouble, but the statistics do not suggest that the size of the dose has any such effect. The organisms of rheumatism were probably present in the myocardium, endocardium, or pericardium in these cases, and the salicylates (in the doses usually given) appear to have had no action in preventing their entrance into the heart, nor in stopping their further activity when once established there. This is confirmed by their inability to check the continuance of that low intermittent fever, with its daily or almost daily rise, usually to some point between 99° and 100° F. (37.2° and 37.8° C.), so characteristic of rheumatic infection in childhood. Cockayne (*Quarterly Jour. of Med.*, April, 1911).

Moderate doses of **salicylate**—10 to 20 grains (0.6 to 1.3 Gm.) four-hourly—are quite as effective as very large doses. Twenty or 30 grains (1.3 or 2 Gm.) of sodium bicarbonate should be given with it, and the bowels be kept open by saline aperients given at fixed intervals. The drug should be left off gradually when the active period of infection seems to have ceased. C. F. Coombs (*Prescriber*, May, 1911).

**Aspirin** tends to aid the above agents, and has been found effective alone in some cases.

**Aspirin** tried in 35 consecutive instances of chorea. Inasmuch as the mild forms of the disease have a tendency to recover without treatment in from six to ten weeks, conclusions require a certain amount of reserve. In mild cases the aspirin seemed to be of service, but other drugs have proven equally valuable. In severe cases the drug in from 10- to 15-grain (0.65 to 1 Gm.) doses, given three or four times a day, is of value. Aspirin cannot be considered as a specific of chorea, but it is well worth trying, particularly in severe cases. It is best given in powders in

water to which a little lemon juice has been added. R. T. Williamson (*Lancet*, No. 4173, p. 526, 1903).

The writers tried **aspirin** in ordinary and severe cases of chorea with good results. At first they gave from 3 to 5 Gm. (45 to 75 grains) daily (the patients varied from 10 to 15 years), and reduced it to 2 to 3 Gm. (30 to 45 grains) later. Good effects were noticed as early as the second day, and chiefly showed themselves in the direction of lessened disturbance in the movements of the mouth and head, so that feeding became much less troublesome and some sleep was obtained. Treatment varied from fifteen to twenty-five days in duration. The authors were particularly impressed with the value of the drug in their 4 severe cases, and believe that no other remedy as yet proposed is as effectual. Mas-salongo and Zambelli (*Gaz. degli Osped.*, Jan. 21, 1906).

The writer classes chorea minor among the acute infectious diseases, and notes the close relationship of this disease to acute articular rheumatism. The portal of entry for the specific cause is presumably the nasopharynx and tonsil, as is the case in epidemic meningitis and anterior poliomyelitis. This indicates the importance of insisting on thorough and regular **cleansing of the mouth and pharynx** of the patient with antiseptic gargles and mouth washes. In chorea minor the symptoms of an acute infection are limited to the first few days in the form of moderate fever and occasional sore throat, the fever itself needing little or no treatment. The advent of acute articular symptoms or cardiac involvement calls for special treatment. In associated articular conditions the writer has found no influence on the course of the disease from the use of **salicylates** or **aspirin**. On the contrary, these drugs in children often cause physical and mental discomfort. **Psychic treatment** is of the utmost importance. The absence

of all exciting influences, absolute rest of both body and mind, and isolation in severe cases are essential. The diet should be soft or liquid, given frequently in small quantities. J. Grober (*Deut. med. Woch.*, Bd. xxxviii, S. 833, 1912).

**Thyroid gland**, in small doses, 1 grain (0.065 Gm.) three times a day during meals; **pituitary gland**, or **parathyroid gland**, all of which enhance oxidation, and **antitoxin**, owing to its antitoxic properties, have been used advantageously in this class of cases. **Horse serum** is also being tried.

Case of a girl aged 10 years who had shown marked choreic phenomena at frequent intervals for a period of three years. After ineffectual treatment successively with arsenic, saline aperients, nourishing and non-irritating diet, potassium iodide and bromide, salicylates, and quinine, temporary improvement occurred under the influence of **brine baths**. The condition having lately become worse than at any time before, a fluidextract of **thyroid gland** was ordered in teaspoonful doses twice daily. The child showed marked improvement and returned to school in the second week. The thyroid was continued for two months, with the dosage reduced to 1 dram (4 Gm.) a day in the second month. At time of writing there were no signs of chorea, the improvement having been maintained for over nine months. P. A. Roden (*Lancet*, Oct. 29, 1910).

Report of 6 cases of chorea which gave a history of previous tonsillitis and 4 of rheumatism. Upon **removal** of their **tonsils**, uniformly favorable results were obtained. Not only was their general health markedly improved, but the choreic movements ceased and did not recur. A. Archibald (*St. Paul Med. Jour.*, Nov., 1914).

The writer connects the thymus gland with process as a result of the morbid effect of acute infectious dis-

eases upon this organ. He found the **salicylates** followed by **thymus gland** especially efficient, the movements having been found to subside promptly after the latter had been given alone. Haneborg (*Norsk. Mag. f. Laegevedensk.*, Aug., 1916).

Intrathecal injections of **horse serum** have been instrumental in gaining striking and rapid improvement in most of the cases so treated by the writer. Only in the mild cases was twitching entirely absent after 2 weeks, and all 3 of these 7 patients had been affected for at least 3 weeks before treatment was inaugurated. One patient, a girl (a mental defective with a neurotic heredity), showed absolutely no reaction to the injections of serum. The most striking results followed the use of the horse serum in the maniacal and very severe cases. On the whole the results obtained do not encourage the hope that this is any advance on other methods of treatment. Undoubtedly the use of horse serum is of great value in controlling the very severe cases, but one would not choose to use horse serum in the treatment of any moderately severe, or mild case. Porter (*Amer. Jour. Dis. of Children*, Aug., 1918).

**Autosera** have recently been tried with some degree of success.

The writer recommends Goodman's treatment which consists in the injection, 1 to 4 times, of the **patient's own serum** into the spinal subdural space. Disappearance of the choreic movements occurs frequently within 3 days, or even less, and a majority of cases remain permanently free of movements. Certain instances of recurrence are mild and readily amenable to another injection. Faber (*Calif. State Jour. of Med.*, Jan., 1917).

Goodman's autoserum treatment was used by the writer in 100 cases. In 5 per cent. recurrence took place within a year, giving 95 per cent. of successful cases. In this method 50 c.c. (1½ ounces) of blood is with-

drawn from the arm and rapidly centrifugalized, after which the serum is pipetted off and placed in the incubator at body temperature. A lumbar puncture is performed and 20 c.c. (5 drams) of spinal fluid withdrawn; the serum is slowly injected at body temperature, taking from 5 to 8 minutes. The patient is kept in bed in the recumbent position for several hours to prevent heart collapse and the injection is repeated in 5 or 6 days if necessary. Many cases show on the following day a slight rise in temperature, vomiting, increase in pulse rate, and perhaps a slight stiffness of the neck; these symptoms are, however, not serious. Patients with syphilis, tuberculosis, or enlarged thyroid do not do well under this method. Care must be taken to keep the patient in bed for 4 or 5 days previous without medication of any kind, as a saturation of the nervous system with chloral, bromides, or arsenic may result in collapse when the serum is injected. R. D. Moffett (Med. Rec., Sept. 8, 1917).

The writer injected into the lumbar cord region about 20 c.c. (5 drams) of blood serum obtained from 50 c.c. (1½ ounces) of blood withdrawn from the median basilic vein. Of 23 patients so treated, 77 per cent. were cured, 19 per cent. improved and one unimproved, this one having refused further treatment on account of a severe reaction. There has been no recurrence so far. In all instances, except 6 in which tonsils were removed, there were what seemed to be foci of infection, which were attended to after the course of treatment. Of the 23 cases, 17 were of a mild degree and 5 were severe. Brown, Smith and Phillips (Can. Med. Assoc. Jour., Jan., 1919).

In cases which resist other measures intraspinal injections of **magnesium sulphate** might be tried.

Four cases of severe chorea in which the duration of the affection

was aborted. There has been no recurrence since the treatment by intraspinal injections of 3.5 c.c. (56 minims) of a 25 per cent. solution of **magnesium sulphate**. The patients were girls between 12 and 22 years old. The action of the drug was apparent in a few hours, the symptoms subsiding completely in some, but requiring a second injection in the others. Slight by-effects were noted, but they were transient in all, and in the 40 cases on record in which the magnesium sulphate has been administered in intraspinal injections apnea was observed only in 1 case, and it was brief and transient. The tendency to headache and pain in the limbs after the injection can be reduced by a preliminary injection of morphine. G. Marinesco (Semaine médicale, Nov. 18, 1908).

The writer obtained good results from a single injection subcutaneously of 15 c.c. (4 drams) of a 10 per cent. solution of **magnesium sulphate**. Urdiates (Revista de Med. y Cirurgia Practicas, Dec. 14, 1916).

Especial attention should be given the intestinal tract and stomach, renal disorder, or any state of autogenous poisoning, anemia, malarial poisoning, the presence of intestinal parasites, etc.

The writer has noted a relation between helminthiasis and chorea. In a case recently observed, microscopic examination revealed ova in the feces, and the administration of **anthelmintics** was followed by the expulsion of 3 ascarides and many segments of *tænia solium*, with the result that there was entire abolition of choreic symptoms. M. de Luna (Gaz. degli Osped., Jan. 12, 1902).

Two cases of chorea with *tænia solium*. The first case was that of a girl aged 17 years, but looking very much younger. Her illness was of five days' duration, the movements beginning upon the right side, but rapidly becoming generalized. She had had a slight choreic seizure four years before. The patient's move-

ments became so violent that at times she had contrived to throw herself out of bed upon the floor. Under the ordinary treatment with salicylate of sodium there was no improvement until, the possibility of tapeworm being considered, a dose of **male fern** was administered, and a large *tænia solium*, without the head, was expelled. From this time she continued to improve, and after the expulsion of a large number of segments with the head, following another dose of the anthelmintic, she made a prompt and complete recovery. In the second case, that of a girl aged 12 years, expulsion of a complete *tænia solium* of fair size under the same treatment caused disappearance of the symptoms almost immediately. The possible presence of a tapeworm should always be borne in mind in those cases which are not amenable to the usual routine treatment. James Burnet (Brit. Jour. of Children's Dis., April, 1904).

The use of morphine, chloral, chloroform, or other depressants for the suppression of the muscular movements is of questionable propriety in any case, and will usually prove injurious.

After recovery from chorea especial care should be exercised in the education and bringing up of the child. A display of good judgment and the intelligent direction of conduct and development will be well repaid in increased stability and safety from relapse or from the subsequent occurrence of some other and more serious neurosis.

The treatment of *chorea insaniens* is practically the same as that of an outburst of acute mania. Active measures—eliminants and nerve sedatives—are indicated.

### ANOMALOUS VARIETIES OF CHOREA.

The other conditions described under the name of chorea are:—

**Endemic chorea, or epidemic chorea,** a form of acute chorea with hysterical symptoms which develops in a number of persons at or about the same time in the same school or community. Suggestion plays an important part in its etiology.

**Hysterical chorea:** Closely allied to the above, but with the characteristic symptoms of hysteria superadded. The so-called "chorea major" is a purely hysterical phenomenon, and is not a chorea at all.

**Electrical chorea,** also known as **Dubini's disease,** is the name given to certain forms of acute chorea in which the movements are sudden and lightning-like in onset, and also to a state in which sudden rhythmical muscular contractions occur, simulating a "*tic co-ordiné*." The term is loosely employed, and is used in a different sense by different authors.

**Procurive chorea,** or "**chorea festinans,**" is a form of chorea with hysterical accompaniments in which rhythmical dancing and procurive movements are prominent, vertigo being often present at the same time.

**Saltatory spasm** is a choreoid affection sometimes occurring in epidemics, and characterized by peculiar jumping and dancing movements, which are executed when the patient is startled in any way. It is closely related to the forms of muscular clonic spasm affecting a few or many groups of muscles of the body to which the name "*tic convulsif*" is given. It is also spoken of as "*lata*." It occurs in degenerates of hysterical tendencies, is often accompanied by the unconscious and involuntary repetition of words and phrases and actions seen or heard, and by the involuntary repetition of obscene words.

**Oscillatory or nodding spasm,** spas-

*mus nutans*, is characterized by rhythmical wagging or nodding movements of the head occurring in paroxysms or continuing for hours, or even during the entire time the patient is awake. It occurs in extreme degenerates, and may be complicated with epilepsy or other neurosis, or may accompany a hemiplegia or other secondary degeneration. It shades imperceptibly into "habit chorea."

**Tic co-ordiné**, or **habit chorea**, consists in the involuntary occurrence of tricks of speech or gesture—a twist of the head, shrug of the shoulder, etc. It is sometimes a result of an early attack of acute chorea, but occurs also as a primary affection, and may be inherited.

**Posthemiplegic chorea** is a name given to the irregular rhythmical or arrhythmical jerky movements sometimes seen in hemiplegic limbs. Similar movements may occur as a result of infantile cerebral palsies.

**Chronic adult chorea**, also known as **Huntingdon's chorea**, is characterized by choreic movements associated with spastic symptoms and progressive mental deterioration. There is always marked degeneration in cortical cells and in pyramidal tracts.

In Huntingdon's chorea mental symptoms ending in dementia are an essential factor in the disease. Post-hemiplegic tremor is frequently called chorea. Hysterical chorea is a different condition and has the mental symptoms of hysteria. The tremor of paresis may cause it to be mistaken for chorea. Burr (*Jour. Nerv. and Ment. Dis.*, June, 1908).

If there is a history of chorea in ancestry this "chronic adult chorea" is called "Huntingdon's" or "hereditary chorea." The affection was described during the middle of last

century, but has obtained general recognition only since Huntingdon, an American practitioner, called attention to it in 1872. In typical cases the disease develops insidiously, slowly progresses, and terminates in marked spastic paralysis with advanced dementia, or in death. It is closely related, in etiology, pathology, and clinical features, to general paresis, into which it probably shades by insensible degrees.

Two cases of the rare affection known as Huntingdon's disease or hereditary chorea. The first patient was a man of 43, free from known hereditary or pathological taint until the first onset of the chorea five years ago. The twitchings and motor disturbances interfered to some extent with voluntary movements, but had not incapacitated the patient, although the attention and memory did not seem quite as alert as usual. The affection seemed of the Huntingdon type except for the absence of known inherited taint. The other patient was a man of 66, the father of several healthy adult children. The chorea had begun at the age of 46. The mind had not failed to a notable extent, although there were occasional periods of excitement with tendency to suicide. The writer mentions as a characteristic symptom the loss of the function of arresting one motor impulse and substituting for it an opposite one—*adiodokinesia*. De Castro (*Jour. Amer. Med. Assoc.*, from *Brazil Medico*, May 1, 1912).

A study of 4 family complexes, showed that 962 cases of Huntingdon's chorea could be traced back to some half-dozen persons, including 3 (probable) brothers who migrated to America during the 17th century. Among the 3000 odd relatives of the 962 choreics, many nervous traits are recorded—epilepsy 39 times, infantile convulsions 19 times, meningeal inflammations and brain fever 51 times, hydrocephaly 41 times, feeble-mindedness 72 times, Sydenham's chorea 11 times, and tics 9

times—mostly in one small family. Davenport and Muncy (Amer. Jour. of Insanity, Oct., 1916).

Case which illustrates the hereditary nature of the disease. The patient presented the developed form of the disease, while the patient's father presented the *forme fruste*. Two of his sisters and 2 of his own children also showed the latter. One brother, 1 sister, and his daughter, on the other hand, showed the developed form as he did. L. Grimmer (N. Y. Med. Jour., Jan. 27, 1917).

These forms of choreic movements with degenerations in brain and cord are, of course, incurable.

Huntingdon (Med. and Surg. Reporter, April 13, 1872) stated that the disease can neither be cured nor ameliorated and this corresponds to the view of practically every other writer. Riesman (Amer. Jour. Med. Sci., vol. cxiv, No. 2, 1897) reported 20 per cent. of cures, but it is certain that not all of his cases belong under the heading of chronic progressive chorea as that term is employed in this article. Herringham ("Brain," 1888) reported 11 cases of chorea in the aged with recovery, but these were probably cases of chronic minor chorea. Fry (Jour. Nerv. and Ment. Dis., Sept., 1891) reported a case of chronic chorea with cure at 69, but thought it was a simple chorea in an aged person. Gowers ("Dis. of Nerv. System," 2d ed., vol. ii) quoted a case with recovery after the use of arsenic. Lange (Berl. klin. Woch., Feb. 5, 1906) thought there was some improvement in his patient following confinement in a hospital. Though the condition of a number of the writer's patients varied from time to time, no treatment had any permanent effect. While the prognosis is unfavorable, therefore, death is usually long delayed and is finally often due to some intercurrent disorder. A. S. Hamilton (Amer. Jour. of Insanity, Jan., 1908).

Derangement of metabolism is the cause, depending upon a diseased

nervous system. The writer reports 3 cases; in 2 of these he was able to follow up the disease through 4 generations. He concludes his study with Huntingdon's statement: "I have never seen a cure or an improvement of the symptoms in this form of chorea; once started it will lead without fail to a fatal ending." Weber (Präger med. Woch., May 16, 23, 30, 1912).

It will be seen that the term chorea has been applied to numerous and widely different affections, insuring some confusion, as previously remarked. It is unfortunate that the name of "chorea" cannot be entirely restricted to mean the acute or Sydenham's chorea, since this is a tolerably well defined group of clinical symptoms, with a definite course and character. The other varieties of chorea are symptoms of hysteria and extreme degeneracy or of chronic degeneration in motor cells and tracts, and should preferably be relegated to their proper nosological place.

H. O. Waters noticed in 1 of his patients that the movements ceased temporarily under the influence of all kinds of **instrumental music** except that from the common jew's-harp. In a case seen by the writer the church organ had a remarkably quieting effect which lasted about an hour. He now reports a third case in which the music of a violin had a quieting effect. It became a regular practice for a fellow patient to play a few strains of music before he attempted to eat his meals. It was not uncommon for him to throw himself from bed or nearly so unless soothed by music. Clarence King (N. Y. Med. Jour., Aug. 12, 1916).

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**CHORIOEPITHELIOMA.** See  
ABORTIÓN.

**CHOROID, DISORDERS OF.**

See IRIS, CILIARY BODY, AND CHOROID: DISORDERS OF.

**CHROMIDROSIS.** See SWEAT GLANDS, DISEASES OF.

**CHROMIUM.**—Chromium is one of the metallic chemical elements. It does not occur in the free state, or very abundantly in nature, but is usually found as chromite. Chromii trioxidum U. S. P. (chromic acid) and potassii dichromas (potassium dichromate) are the chief derivatives which are used in medicine. Chromic acid is an anhydride, and occurs as fine rhombic crystals of a deep-red color. It has an acid, metallic taste, is very deliquescent, and is soluble in water. Potassium bichromate also occurs as fine, crimson, needle-shaped crystals, and is soluble in water. It should not be combined with alcohol, ether, or sweet spirit of niter, as explosions are very apt to occur.

**PREPARATIONS AND DOSE.**

—The official preparation of chromium is:—

*Chromii trioxidum* U. S. P. (chromic acid), which is used only locally. It may be employed in as strong a solution as 100 grains to the ounce of water (6.5 Gm. to 30 c.c.), but a 5 per cent. solution is generally used.

*Potassii dichromas* (potassium dichromate), which is no longer official, has been given internally in doses of from  $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.006 to 0.012 Gm.).

**PHYSIOLOGICAL ACTION.**

Chromic acid possesses the power of killing all low organisms, oxidizing organic matter, coagulating albumin, and destroying the tissues with which it comes in contact. It is thus antiseptic, disinfectant, and powerfully caustic. Made into a paste with

water, its action is exceedingly slow and gradual, but deeply penetrating; in saturated solution it is less penetrating and slower in action. By employing a solution more or less dilute, the action may be graduated according to the effects desired. Death has resulted from absorption when it has been applied too freely. Its local effects are, for the most part, antagonized by bland neutral fats applied in excess. The toxic effects are similar to those of potassium bichromate.

Potassium dichromate, when applied locally, causes dangerous ulcers of the skin, and workmen handling cloth dyed with solutions of this drug are apt to suffer from ulcers and eczema. Like the trioxide, it is an energetic oxidizer.

**POISONING.**—Chromic acid and potassium dichromate are both violent corrosive poisons when taken internally, and symptoms may occur, due to absorption, after their too free external use. The symptoms of poisoning are those of a violent gastro-enteritis. Should poisoning occur, emetics, demulcent drinks, and dilute alkalies should be administered.

Case of a young woman who had a mass of vegetation covering the vulva which resisted the usual methods. The writer decided to cauterize it deeply with chromic acid. A solution of the acid, 100 grains (6.5 Gm.) to the ounce (30 Gm.), was applied, and rather less than  $\frac{1}{2}$  ounce (15 Gm.) of this solution—about 50 grains (3.25 Gm.) of the acid—was used up. After coming from under the anesthetic, the patient complained of great pain in the vulva; about six hours later the writer was called to see her, and found her with a very rapid pulse, nausea, and great thirst. He ascribed this condition to the ether, but



when called to see the patient early the next morning he found her condition alarming. She was very restless, and frequently called for water, which was immediately vomited; face was pale, extremities cold, skin covered with profuse perspiration, and there was fear of approaching death. She remained conscious.

The writer then saw that he had to deal with a case of chromic acid poisoning, and used very active stimulating treatment. The dressings were removed, and the vagina douched, for fear some of the acid solution might have entered in spite of care, but the mucous membranes showed no evidence of this.

The patient remained in this extreme condition for about thirty-six hours, after which she gradually returned to her normal state, and, after two weeks, was able to leave her room.

A few years ago J. Wm. White, of Philadelphia, reported a case similar to this one, but with more disastrous results. His patient was a healthy girl. Twenty-seven hours from the time of the application of the acid she died of chromic acid poisoning. He used the same strength solution, 100 grains (6.5 Gm.) to the ounce (30 Gm.)

John Marshall made a chemical analysis and reported that the kidney-tissue and liver-tissue both contained chromium, most likely as sodium chromate—known to be poisonous in doses of from 1 to 3 grains (0.065 to 0.2 Gm.). J. W. Shaw (*Va. Med. Semi-Monthly*, vol. v, No. 21, 1901).

Case of a young woman aged 22 years who had made numerous attempts to commit suicide. She finally poisoned herself with from 20 to 25 Gm. (5 to 6¼ drams) of potassium bichromate. About three or four hours after taking the drug she felt some pain, and two hours later she was brought to the hospital. There was a greenish mucus coming from the mouth, the pupils were dilated, the pulse was rapid, the respirations were more frequent, but

there was no vomiting. The stomach was washed out and contained a greenish fluid. During the washing there was an involuntary evacuation of the bowels that was not particularly characteristic. Later, the patient began to vomit; there were persistent diarrhea and extreme nervousness. She gradually grew weaker and finally died. There was chromium in the bowel movement, the vomitus, and the liquid obtained by washing. At the autopsy the mucous membrane of the intestine was red. The salt was taken inclosed in figs, a fact which explained the absence of any change in the mucous membrane of the mouth. Berka (*Münch. med. Woch.*, April 21, 1903).

Case of poisoning in a woman 42 years of age who took between 2 and 3 tablespoonfuls of battery fluid containing bichromate of potash and a small quantity of sulphuric acid. Shortly after the ingestion of the fluid vomiting occurred, and two hours later there was severe pain in the stomach. The patient was clear mentally. The stomach was immediately washed with 40 liters (quarts) of sterilized water, followed by the injection of 3 liters (quarts) of a 1 per cent. solution of nitrate of silver. After this was removed the whites of 10 eggs were introduced into the stomach. One hour later the patient collapsed and received a subcutaneous injection of 600 c.c. (20 ounces) of physiological salt solution. A blood examination showed a polynuclear neutrophilic leucocytosis. There was albumin in the urine, red blood-cells, and other evidences of kidney inflammation, and on the third day sugar was found, the amount being 0.15 per cent. In a few days the glycosuria disappeared and the patient was discharged recovered.

The writer refers to a number of cases of poisoning by battery fluid, the symptoms of which are due to the bichromate of potash. In a few of them other mixtures, such as sulphuric acid or sulphate of mercury,

possibly played a part. In most of them a glycosuria developed, the promptness and severity of this symptom determining the gravity of the poisoning. In most of the cases so far reported there has been a fatal termination. A. Lohr (Berl. klin. Woch., July 11, 1904).

Case of attempted murder by poisoning with potassium bichromate, a drug rarely used for such purpose, but few cases having been reported. The patient, a woman of 58 years, was given the poison in port wine, and in a mixture of alcohol with raspberry syrup. Later, her husband prepared her a strong solution of the chemical in water, calling it "tea." The woman took altogether about 6.5 Gm. (100 grains). At first she vomited heavily, had convulsions, pains in the stomach, dizziness, headache, cold sweats, and diarrhea. Her face became ghastly pale, eyes dilated; respirations very slow and labored, about 8 to 10 per minute; pulse 56, weak and compressible. Urine contained considerable blood. The woman recovered after a week, but complained of occasional pains in the stomach and of backache; for some time albumin was found in the urine. The writer recommends, as treatment, **alkalies** and **milk** to counteract the irritating poison, and **anodynes** for the pain. Francis E. Fronczak (Amer. Med., March 5, 1905).

**THERAPEUTICS.—As an Antiseptic and Disinfectant.**—Two drams (8 Gm.) of chromium trioxide added to 4 or 5 quarts (liters) of water gives an inexpensive, but efficient, antiseptic and disinfecting lotion for **leucorrhæas**, **ozenas**, **hyperidrosis**, **putrid sores**, etc.; a lotion of 10 grains (0.65 Gm.) to the ounce (30 Gm.) has a decided effect upon **syphilitic**, **gouty**, and kindred **maladies of tongue and throat**. As a local application to **cancerous** and other **ulcerations**, it is preferable to all other caustics, since

the pain attendant on its application is trifling; but it must be used cautiously and discriminatingly.

**Morbid Growths.**—A concentrated solution is useful in removing **syphilitic condylomata** and **warts** and other morbid growths from the genital region. It has been applied to **external** and **bleeding hemorrhoids**, to **fungus hematodes**, **onychias maligna**, and **onychias parasitica** with great benefit. **Warts** quickly yield to the application of chromic-acid crystals, after the surface of the growth has been slightly moistened.

**Diseases of the Air Passages.**—But the greatest availability appears to be in treating diseases of the throat, upper pharynx, and nose. Owing to its hygroscopic character, no agent is so effective when applied to **nasal polypi**, and it is also highly recommended in **hypertrophic rhinitis**. In either case the most convenient method is to heat the tip of an ordinary probe and touch it to one of the acicular crystals of acid; enough adheres for two applications, but care must be taken not to overheat the instrument, lest decomposition of the chromic anhydride should occur, and an insoluble compound be formed.

**Internal Use.**—The use of the acid and potassium dichromate has not met with favor, mainly owing to the toxicity of these salts. Kolipinski has warmly advocated the use of *chromium sulphate*, however, which he states is non-toxic. He administers it in doses of from 1 to 8 grains (0.065 to 0.5 Gm.); 30 to 40 grains (2 to 2.6 Gm.) at one time result in no unusual sensations, except a very mild vertigo or lightness in the head. A 4-grain (0.26 Gm.) tablet or pill is the most convenient form, given after meals. Oc-

casionally the unabsorbed residue colors the feces. Chromium sulphate dissolves in water very slowly. No unpleasant by-effects were observed in patients who had taken it continuously for as long a period of time as four or five years.

The diseases in which chromium sulphate was used with success by Kolipinski were **mammary cirrhosis**, the **menopause**, functional **impotence** in men, **chronic alcoholism**, nervous **vomiting** and **vomiting in pregnancy**, **neurasthenia**, **tabes**, **exophthalmic goiter**, and the **migraines**.

Results obtained from chromium sulphate are speedy and striking. In **neurasthenia** it not only is curative, but dispenses with all treatments by rest, travel, diversion of mind, dietetics, and physicomchanics. In **exophthalmic goiter** the rapid pulse and cardiac phenomena are reduced to nearly normal; the pulse remains so. The nutrition of the body is bettered; the trembling ceases; likewise the state of nervous erethism and irritability. The bulging eyes and struma recede slowly. The cases treated were mostly old, neglected, or mismanaged ones.

Chromium sulphate is helpful in the second stage of **tabes** by removing the inco-ordination of muscles. The **staggering walk** and the **unsteady motions** of the hand, the **paralytic weakness** of vesical and rectal sphincters, are overcome. In the third stage decided improvement is obtained. The **ataxia** in its various forms disappears. **Tabetic pains** require no other medicinal treatment. Diminution of sensation, tactile pain, touch and temperature senses are gradually overcome if obtunded; **anesthesia** also. Louis Kolipinski (Mo. Cyclo. of Pract. Med., Sept., 1908).

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**CHRYSAROBIN.**—This drug is the active principle of a powder derived from the wood of the tree *Andira araroba*. The powder, known as **goa powder** in the East Indies, was first used medicinally in Brazil. It contains about 65 per cent. of chrysarobin. Chrysarobin is a yellow, tasteless powder, insoluble in alcohol and water, but soluble in ether, acids, and solutions of the alkalis.

Sometimes confused with chrysophanic acid, chrysarobin is a neutral principle distinct from the former, into which it is converted, however, upon oxidation. The acid is far less irritating than chrysarobin itself. Chrysarobin of poor quality is apt to contain a large proportion of chrysophanic acid.

#### PREPARATIONS AND DOSE.—

*Chrysarobinum* (chrysarobin) may be given internally in the dose of  $\frac{1}{2}$  grain (0.03 Gm.). The *unguentum chrysarobini* (ointment of chrysarobin), which is of 6 per cent. strength, should be mixed with several parts of benzoinated lard before applying, as it is too strong for direct use.

**PHYSIOLOGICAL ACTION.**—Chrysarobin is a violent irritant poison. Large doses cause irritation of the mucous membrane of the stomach and intestines, producing severe attacks of vomiting followed by purging.

Applied locally the drug, when used for a long time, produces a dermatitis, and if used too strong causes intense swelling and inflammation of the skin, followed by desquamation. It also causes a yellowish color of the urine, which turns red upon the addition of alkalis. It is a parasiticide and cathartic. One disadvantage of the drug is that it stains the skin and clothing a dark-brown color, and should not, therefore, be used upon the face. This color can be removed by a weak solution of chloride of lime.

The action of chrysarobin upon skin lesions has been ascribed to a removal of oxygen from the tissues.

Chrysarobin plaster causes a homogenization and necrosis of the granular and part of the prickle-cells of the epidermis, with pigmentation of the lower cornified strata. If used in greater strength there will be edema and severe inflammation of

the cutis and intra- and inter-cellular edema of the prickle-cells of the epidermis, with the formation of seropurulent vesicles. Below the necrotic layers a new and more extreme layer of prickle- and granule-cells will develop. M. Hodara (Monats. f. prakt. Dermat., Sept. 15, 1900).

The elimination of chrysarobin, applied internally or externally, does not proceed by way of the kidneys. Only minimal amounts are eliminated in the urine and consequently there is little if any danger of nephritis from this cause. Winkler (Correspondenz-Blatt für schweizer Aerzte, Sept. 15, 1907).

**THERAPEUTICS.**—This drug is one of the most useful in **psoriasis**. It may be given internally in  $\frac{1}{2}$ -grain (0.03 Gm.) doses three times a day, but it is employed chiefly externally, often in the form of an ointment composed of 1 dram (4 Gm.) of chrysarobin to 1 ounce (30 Gm.) of benzoinated lard.

The transitory application of chrysophanic acid to the skin produces no reaction; but if it be applied to the same spot for several days in succession, about the third or fourth day an erythema appears, accompanied by more or less smarting of the place touched. In psoriasis one hopes to see this chrysophanic erythema, for, as Godart says, "No erythema, no cure." The erythema appears most readily in individuals with a damp, moist skin, especially if the part touched be rich in sweat-glands. Pouchet and Godart offer the following explanation of this: The sweat, if examined at the time of its emission, is found to be of an acid reaction. This acidity is due to a volatile fatty oil which rapidly evaporates, and gives place to an alkaline reaction. The sweat, having become alkaline, plays the part of an alkaline solution in which we know chrysarobin is readily soluble, and so the presence of erythema is a proof that the drug is commencing to act. A practical point arising from this is to forbid the use of any soap

or alkaline bath when once the erythema has started, or the erythema and irritation may become universal. The red color, vivid at first, becomes violet, then brown, and finally the epidermis exfoliates as fine furfuraceous scales. Pautrier (Rev. prat. des mal. cutan., syph. et ven., Oct., Nov., and Dec., 1903).

Chrysarobin is still the specific in **psoriasis**. A generous use of chrysarobin siccatives and of ointments containing, besides chrysarobin, oleate of lead is to be recommended as an especially quick and thorough treatment of psoriasis. Unna (Brit. Med. Jour., Nov. 19, 1910).

Robinson recommends its use in **alopecia circumscripta**. The ointment is also used in **chronic acne** and **vegetable parasitic diseases** with good results. H.

**CHYLOTHORAX.** See PLEURA. DISEASES OF.

**CHYLURIA.**—**DEFINITION.**—A peculiar condition of the urine in which it presents a milk, or chylous, appearance and contains the constituents of chyle, especially fat and albumin.

**VARIETIES.**—Two varieties of chyluria have been observed: (1) the tropical chyluria, which is of parasitic origin; (2) the non-tropical chyluria, the cause of which is unknown.

**SYMPTOMS.**—Chyluria presents an extremely varied clinical history, and the descriptions given of cases are most diverse. Its course is marked by an irregularity and capriciousness which cannot be explained. The only constant symptom is the presence of so-called chylous urine. This fluid usually presents a peculiar whitish, opaque, milky appearance; sometimes the color is not whitish, but pink from the presence of blood. Occasionally the blood is not intimately mixed with the urine and very soon forms an adherent coagulum at the bottom of the vessel. In many cases the urine, after some standing, will form a superficial stratum resembling cream or *blanc-mange*. The odor of the urine is ordinarily acid, rarely urinous; its reaction acid or neutral, rarely alkaline. Chylous urine ordinarily decom-

poses speedily and will then smell of sulphureted hydrogen. Sometimes it has been observed that chylous urine could be kept for months without fermenting. The specific gravity of the urine as well as its appearance varies greatly in the same person at different times, even at different periods of the day. The urine may, in some cases, contain coagula before evacuation, which may cause local disturbance and pain while it is being passed. When blood-serum is added to chylous urine, large coagula will ordinarily form.

Microscopic examination of the urine shows that it contains fat in molecular form, but milk-globules or large drops of fat are not seen; the urine further contains leucocytes and blood-corpuscles, both white and red. In some cases crystals of uric acid have been observed; when the reaction of the urine is alkaline, the characteristic crystals of phosphate of ammonia—magnesia—are observed. Frerichs relates that in 1 case he found the urine to contain a multitude of ripe and unripe spermatozoa. In the tropical variety of chyluria, Lewis, in 1870, and after him many other investigators, found the embryos of *Filaria sanguinis* in the urine.

By shaking the urine with ether, the fat molecules are dissolved and the urine clears up, completely or partially. Besides, the ordinary fat-cholesterin and lecithin have also been found.

Chylous urine always contains albumin, generally in the form of serum-albumin; but globulin, albumose, and peptone may likewise be present. Casein has never been observed; sugar is not ordinarily contained in chylous urine, but Pavy and Habershon are said to have found it in 1 case.

Quantitative estimations of the contents of chylous urine have been made in great number; the amount of fat varies from 0.028 to 3.3 per cent., while the albumin was found in a quantity of 0.12 to 2.7 per cent. As may be seen, their relative proportion varies much.

The discharge of chylous urine usually occurs very suddenly; it may be constant, but more frequently is intermittent. The chyluria may cease for months and years and reappear without appreciable cause, even if the patient has made a complete

change of climate. The urine is, in many cases, chylous only in the early hours of the day, or presents, at that time, a much larger quantity of chyle than at other periods of the day. This intermittence has been observed as well in the tropical as in the non-tropical varieties of chyluria. In some instances the position of the body—recumbent or erect—is found to bear influence. Vickery reported the case of a man 57 years old who had been in Florida for a while. He could bring on a chyluria by lying down an hour, especially if he lay on the back rather than on the side. The *Filaria sanguinis* was found in his blood.

Case of familial European chyluria in a man of 19. He complained of constant pain in his back at the level of the twelfth dorsal vertebra, also headache. His father and father's father had suffered in the same way. He had diphtheria with fever of 103.5° F., and mitral insufficiency. The angina soon passed off, but the temperature remained high. The case suggested sepsis, but no cause could be found. The sudden passage of milky urine threw light on the affection, which had become a complete riddle. No filariæ embryos could be found in the blood. There are now, including the author's observation, 57 cases on record of European chyluria. It may be due to parasites, an anomaly of metabolism, or the passage of chyle from the lacteals to the urinary passages. Koopman (Nederlandsch. Tijdsch. v. Geneeskunde, Jan. 5, 1918).

In most cases symptoms referable to the urinary organs are noticed, such as pains in the lumbar region, along the urethra, etc. Occasionally the urine coagulates in the bladder, causing pain and difficulty during micturition.

Persons suffering from chyluria may enjoy good health, but generally there is weakness, and wasting, with mental depression. Tropical chyluria is often accompanied by fever and diarrhea.

Chyluria follows a very chronic course.

**DIAGNOSIS.**—Chyluria may resemble pyuria and lipuria; it can be distinguished from both by microscopic examination; in pyuria the urine contains innumerable

pus-corpuscles; in lipuria the fat is not present in molecular form, but in large drops or in fine needles and crystals.

#### ETIOLOGY AND PATHOLOGY.—

The tropical, or parasitical, variety of chyluria is the best known, and its etiology has been elucidated by different authors. It has been observed in the United States, China, Japan, Siam, the Isle of France, Brazil, the East Indies, Egypt, Reunion, Mauritius, Australasia, and recently also in Europe in persons who never had lived in tropical regions. Tropical chyluria is caused by the presence in the blood of the embryos of *Filaria sanguinis hominis*: a nematoid worm.

These embryos were first found in the urine by Wucherer, of Bahia, and later also observed in the blood by Lewis. Their natural history has been elucidated by many observers, especially by Manson.

The adult filaria has a length of from 30 to 40 mm. and is filiform: the embryo measures 0.0075 mm. in diameter and 0.34 mm. in length. Manson found that the parent filariæ live in the lymphatics on the distal end of the glands; they are oviparous and their eggs are arrested in the glands and hatched there. The free embryos then pass along the lymphatic vessels and enter the circulation. Resting in some organ during the day, they circulate with the blood during the night, or, as Mackenzie has shown, they rest during the sleep of their host, whether it be night or not.

Manson describes four varieties of filaria:—

*Filaria nocturna*, which can be detected in the blood only at night.

*Filaria diurna*, which is found in the blood during the day only.

*Filaria perstans*, which is always present in the capillaries.

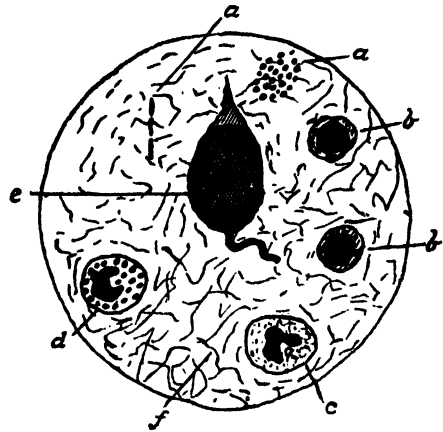
*Filaria Demarquay*, not half the size of the ordinary filaria.

*Filaria diurna* and *perstans* seem to be confined to the western part of Africa, while *Filaria nocturna* is always present in tropical countries and is endemic in some parts of the United States of America. In a study of the blood of about 60 negroes belonging to the different tribes of the Congo States, Firket found embryos of filaria in the blood of the majority of them.

Filaria were also found in the blood of a negro from the Congo who had been living in Belgium for six years.

It has not yet been proved in what manner the embryos of the filaria give rise to chyluria, but it is commonly believed that the parasites obstruct the lymphatics and cause their delicate walls to rupture, or that they perforate the walls of the chyliferous vessels and bring about abdominal communications.

Case reported by the writers which is of special interest in that the parasite itself is not very common in the human family. A fairly thorough search of the literature failed to re-



Drawing of smear of urine, oil immersion. *a*, bacteria; *b*, lymphocytes; *c*, polynuclear; *d*, eosinophile; *e*, parasite; *f*, debris.

veal a case in which this parasite has been found in chyluria. The case reported occurred in a young negro in whom the chyluria appeared two weeks after an illicit intercourse. In the fresh specimen of blood during the first two days of the disease there could be seen a moderate number of the *Cercomonas hominis* (see illustration). As the disease progressed these became less and less frequent, until at the end of two weeks they could no longer be found. The parasites were ovoid in shape, and from one pole projected a filament about half as long as the body of the cell, while from the other pole there projected a short, spine-like process. While the parasite *Cer-*

*comonas hominis* is not infrequent in man and often in a region distant from the alimentary tract, still the probable mode of infection *via* the genitals in this case is, to say the least, unique. C. Rosenheck and G. L. Rohdenburg (N. Y. Med. Jour., Feb. 25, 1911).

It has already been mentioned that chyluria presents an extremely varied clinical history and may be accompanied by divers other symptoms, such as chylurious discharges from various parts of the body, with elephantiasis, lymphangiectasis, etc.

The diversity of the clinical manifestations may, perhaps, find its explanation by the fact that it is not always caused by the same species of filaria.

The non-tropical variety of chyluria is not of parasitical nature, and its origin is, as yet, quite obscure; it occurs even in cold climates, but is a very rare disease.

While in the tropics chyluria is due to filaria in the blood and urine, no parasites are found in the cases reported in Europe. The writers have collected 41 cases, most patients being middle aged, and some of them pregnant. In 3 men traumatism was considered a cause. In some cases the urine was chylous all the time; in others only at times; in still others only the day urine was affected. Blood-corpuscles are found in the urine in Europe, as in the tropics. Their experiments showed that there is a distinct relation between the amount of fat in the intestine and the chyluria, but this is quite independent of any fat injected subcutaneously. Alimentary glycosuria occurs early after increasing the sugar in the chyle. Besides, mononuclear leucocytes are found in chylous urine in large quantities. Franz and von Stejskal (Zeit. f. Heilkunde, Nov., 1902).

Manson's observations seemed to show that the embryos were taken along with the blood in the stomach of a certain form of mosquito, in which they undergo developmental changes. After some days the mosquito discharges its eggs in the

water of some pool and the filaria there becomes free, and by this medium the animals are conveyed to the human system, through drinking the water.

In some cases very small drops of fat have been observed to circulate with the blood and to be discharged through the kidneys; in some instances the urine may be secreted in its normal state, but the fat is added during its passage through the ureters and the bladder. It has been observed concurrently with other diseases, notably pneumonia and renal tuberculosis.

Case of a woman who was admitted to the Presbyterian Hospital suffering from a lobar pneumonia which ran a mild course, and from which she made a perfect recovery. The chyluria appeared ten days after convalescence was established. The patient presented no other symptoms of any kind, and physical examination at present was absolutely negative. The urine was free from casts, contained blood-disks, and no more albumin than was accounted for by the blood. It also contained a moderate number of leucocytes and fat in a molecular form. From time to time she passed urine entirely free from blood. The patient's blood had been examined a number of times, the specimens being taken both at night and during the day, and none contained the *Filaria sanguinis hominis*. These cases of non-parasitic chyluria are of very rare occurrence. F. P. Kinnicutt (Med. Record, April 28, 1900).

The dependence of the chylous change in the urine upon the introduction of fat into the intestinal canal is proven by the disappearance of the fat in the urine under starvation; by the appearance of fat-free urine under a diet very poor in fat; by the excretion of specific fats, such as olive oil colored with sudan red, erucin, lipanin, by the urine following their introduction into the gastrointestinal tract, and by the circumstance that fat which is with difficulty absorbed appears in the measure of its absorability; the lack of relation between the excretion of fat in the urine and

its introduction by other methods, as, for instance, by subcutaneous introduction of colored fat; the early appearance of alimentary glycosuria, caused, probably, by the increased quantity of sugar in the chyle, resulting from the great amount in the intestinal canal; the appearance of chiefly mononuclear leucocytes in the chylous urine. Franz and von Stejskal (*Zeit. f. Heilk.*, Bd. xxiii, ht. 11, Abth. F., ht. 4, p. 441, 1902).

Case of chyluria which depended upon a tuberculous nephritis, the explanation, revealed at the autopsy, being the presence of dilated lymph-channels in the neighborhood of tuberculous ulcerative foci. Chyluria may be due to a number of other causes besides filariasis. Among these are interstitial hepatitis, compression of the superior vena cava or of the portal vein in the presence of peritoneal effusions; also traumatism, cancer, syphilis, and tuberculosis. Giordano (*Riforma Medica*, Nov. 25, 1905).

Case in a man aged 51 years who six years previously had noted that his urine was white and turbid during the winter, while in the spring and summer it became clear. The condition had recurred regularly each winter since then. The only complaints were pain in the back, especially on the right side, and pain on micturition. At times clots were voided. In January, 1908, the patient complained of thirst, loss of weight, and polyuria. Examination of the urine revealed chyluria and diabetes mellitus. The night urine was chylous; the day urine clear. On reclining during the day and sleeping upright in a chair, the urinary finding was reversed. The withdrawal of fat from the diet led to clear urine at night, but the other constituents of chyle, such as albumin and lymphocytes, were still present in the night urine. With increasing quantities of fat in the food, a corresponding increase in milkiness of the urine occurred. Fibrinogen, albumin, and globulin were determined by fractional precipitation

with ammonium sulphate. Cystoscopy revealed the fact that the chylous urine came entirely from the right ureter. The urine was collected from the two kidneys by catheterization of the ureters and analyzed separately. By computation the writer shows that the proportion of fat, albumin, and sodium chloride in the chylous urine corresponded exactly with the composition of chyle as given by Munk and Rosenstein. No ova or embryos were found in the urine, nor was the blood-serum fatty. There are two theories as to the origin of chyluria: (1) that the condition results from direct addition of chyle to the urine, and (2) that the abnormal constituents are derived from the blood, no communication existing between the urinary and lymph passages. A defective catabolism of the chylous material is assumed. If the latter theory were correct, all cases of chyluria should be bilateral. Furthermore, direct communication has been found in a certain number of cases. In two-thirds of all the cases chyluria disappears either in the reclining or upright posture; this would be impossible if the blood condition were the cause of the chyluria. The constant finding of lymphocytes in cases in which centrifugized urine is examined also points to direct admixture of chyle. If one extracts sufficient urine with ether, cholesterin and lecithin are found. Their quantity in the chyle depends largely upon the diet. The absence of glycosuria in chyluria has been urged as an argument against the theory that there exists direct admixture of chyle to urine; but as Munk and Rosenstein have shown, chyle contains about 0.1 per cent. sugar on a fat and proteid diet; 0.3 to 0.4 per cent. after a carbohydrate meal. Only in the latter condition would one expect to find a glycosuria. The absence of clotting in some cases is also without significance, for in certain instances lymph and chyle fail to clot. The writer assumes that in all cases a



direct communication must exist between the lymph-vessels and some part of the genitourinary tract. The absence of chyluria for months and years at a time might be explained by the closure of the opening, the widening of the lymph-vessels, or the establishment of collateral channels. The daily intermissions must be explained on purely mechanical grounds. This explanation of chyluria holds good both for parasitic and non-parasitic cases. Magnus-Levy (Zeit. f. klin. Med., Bd. lxvi, S. 482, 1908).

**PROGNOSIS.**—Chyluria is ordinarily a disease of long duration. Sometimes the patients recover spontaneously; in other cases it leads to anemia and severe diarrhea and the patient dies from exhaustion.

Case of chyluria in which no parasites could be found. The urine suddenly cleared about six weeks later. Salkowski (Berl. klin. Woch., Jan. 14, 1907).

**TREATMENT.**—Medicine seems to have but little influence on chyluria. Rest, good nutritious diet which is not too exclusively animal, the use of pure water for drinking purposes, iron, and quinine have been recommended, as well as large doses of potassium iodide. Against the parasitic chyluria anthelmintics have been tried, as methylene blue (Austin Flint) and thymol (Crombie). In the tropics a plant—*pentaphyllum*—is much relied upon; *man-grove bark* is considerably used in Guiana.

In a case of chyluria reported by Frederick P. Henry, in 1896, the first of the kind observed in Philadelphia, microscopic examinations of the blood drawn from the finger showed that the parasites were very few in number or absent from the blood during the day; they were, therefore, the variety known as the *Filaria nocturna*. Methylene blue in 2-grain (0.13 Gm.) capsules every three hours was ordered. After being taken continuously for seventy-two hours the blood was found to contain actively moving unstained filariæ. The urine and feces were stained a deep blue; the milk was uncolored. After being taken for nine days the drug proved absolutely inert so far as any influence on the vitality of the embryos was concerned, and it did

not stain them until they were dead. Moncorvo obtained prompt recovery in 2 cases of chyluria under the use of ichthyol in daily amounts of 7 or 8 grains (0.45 or 0.5 Gm.), in the form of pills.

Case of chyluria in a man of 58. The night urine was milky and he had recently lost 23 pounds. The day urine was clear, but, on the patient reclining, the urine became at once milky. The milky urine always came from the right ureter. Bacteriological tests were negative and there was nothing to suggest the possible presence of filariasis. A fistula from rupture of a lymphatic into the urinary passages is probably the most frequent cause, although secretory renal chyluria is not an impossible assumption. This case seems to favor the view of a communicating fistula. Treatment along this line was instituted, a silver-nitrate solution being instilled into the ureter and renal pelvis to promote the healing of the assumed fistula. Marion (Annales des mal. des org. génito-urin., Feb. 1, 1910).

Case of chyluria in which 0.6 Gm. (10 grains) of salvarsan was administered hypodermically. The reaction was evidenced only by a rather severe headache and a general sensation of tingling, especially in the fingers, lasting two days. After this injection the urine remained unchanged for the first twenty-four hours; during the succeeding forty-eight hours it became perfectly clear for the first time since the inception of the complaint, seven months before. Suddenly, however, from the sixty-eighth to the seventy-second hour, the urine became markedly chylous and contained large numbers of seemingly dead filariæ of both embryonic and adult forms, the latter so large as not to need a microscope for demonstration, resembling white threads in appearance; after the seventy-second hour the turbidity ceased until at the time of discharge only an intermittent opacity was present, and no filariæ were demonstrable.

Blood-smears taken continuously from the twenty-fourth hour after ia-

jection with salvarsan to the time of discharge, that is, for one week, were all negative as far as finding any filariæ was concerned, whereas before the injection there was no trouble in finding the filariæ in the midnight specimens. P. M. and J. T. Pilcher (Med. Record, Mar. 11, 1911). L.

## CILIARY BODY, DISORDERS

OF. See IRIS, CHOROID AND CILIARY BODY, DISORDERS OF.

**CIMICIFUGA.**—This drug is the root of the *Cimicifuga racemosa*, commonly known as black cohosh, or black snakeroot. The root has a knotted appearance, with many fine rootlets, a faint odor, and a bitter, astringent, acrid taste. It is soluble in water, alcohol, ether, and chloroform.

**PREPARATIONS AND DOSE.**—The following preparations of the drug are official: the *fluidextractum cimicifugæ* (the fluidextract of cimicifuga), the dose being 15 minims to 1 fluidram (1 to 4 c.c.) and the *extractum cimicifugæ* (extract of cimicifuga), the dose being 4 to 15 grains (0.25 to 1 Gm.). The *tinctura cimicifugæ* (tincture of cimicifuga), dose, 1 to 2 fluidrams (4 to 8 c.c.), is no longer official.

**PHYSIOLOGICAL ACTION.**—Hutchinson found that, in frogs, overdoses of the drug were depressant to the sensory side of the spinal cord, causing complete anesthesia, with loss of reflex activity, voluntary motion being preserved. Very small doses of the drug act as a feeble cardiac stimulant. Full doses are depressant to the circulation, causing a fall of arterial pressure, slowing of the pulse, and finally diastolic arrest of the heart. Respirations become slow and are finally arrested. Cimicifuga also stimulates digestion, increases secretions, stimulates uterine contractions, and increases the menstrual flow. Large doses of the drug cause intense headache, giddiness, dimness of vision, dilated pupil, nausea, and occasionally vomiting.

**THERAPEUTICS.**—After arsenic, cimicifuga is the best remedy for **chorea**, especially when used in combination with iron and laxatives. The tincture may be used externally to relieve pain in **rheumatism** and **neuralgia**. It is said to be of value in **chronic bronchitis** when there is free ex-

pectoration, and in **urticaria** of a nervous origin after failure of the usual treatment. It sometimes gives relief in **headache** due to **eye-strain**.

It is also given in uterine conditions, as **amenorrhea**, congestive **dysmenorrhea**, and **melancholia** due to uterine disease. Being a uterine stimulant, it is sometimes substituted for ergot. On account of its tonic effect it is frequently given in the gastric catarrh of **chronic alcoholism**, and is often of value in **delirium tremens**. H.

**CINCHONA.**—Cinchona, cinchona bark, or Peruvian bark, was first brought to Europe from South America some time in the seventeenth century, but just exactly when or how is not really known, though various fanciful tales are extant that purport to account for its introduction. It was certainly employed medicinally as early as 1640, though its most important alkaloid, quinine, was not discovered until 1820. Its name is said to be derived from that of the Countess of Chinchon, wife of a viceroy of Peru, who had been cured of an obstinate intermittent fever by it (Tschirch).

**VARIETIES OF CINCHONA.**—Some thirty-six species of cinchona, of the family Rubiaceæ, are recognized, and, when the number of hybrids is considered, the total is considerably augmented; but only seven constitute the source of the principal "barks" and alkaloids of commerce:—

Red bark, obtained from *Cinchona succirubra*; yellow bark, from *C. calisaya* and its variety *Ledgeriana*; pale, Loxa, or Huanco bark, from *C. officinalis*, the species first discovered; Cuprea bark, from *Remijia purdieana* and *R. pedunculata*; gray, or silver, bark, from *C. nitida*, *C. micrantha*, and *C. Peruviana*; Columbian, or Carthagena, bark, from *C. lancifolia* and *C. cordi-*

*folia*, and Pitayo bark, from *C. pitayensis*. *C. officinalis* was the first species discovered, but the red and yellow barks are now those of chief commercial importance. *C. pitayensis* and the two species of *Remijia* appear to occupy an intermediate position between the true and false cinchonas.

All the cinchonas are evergreen trees or large shrubs that favor mountain ranges and slopes at elevations varying from 400 to 11,500 feet above sea level, 5000 to 8000 feet for the best varieties. The trees average from 30 to 80 feet in height, and measure from 1 to 2 feet in diameter at the base. The leaves resemble those of the laurel, the best being pitted on the under side (except *C. succirubra*), and have a prominent midrib; the flowers are tubular, fragrant, rosy white, or purplish; fruit-capsule two-celled, splitting from the base upward, and containing many winged seeds.

The cinchonas are indigenous to the Andean region of South America, more particularly to Peru, Bolivia, and Ecuador. Red and pale barks, the product of cinchona plantations in India, instituted and fostered by the government, were formerly also obtained in large amount, arriving from Madras and other seaports on the Bay of Bengal. There are likewise plantations in Ceylon, the Malay Peninsula, South Africa, and Jamaica in the West Indies. By far the largest amount of cinchona, however—8½ million kilograms in 1907—is now obtained from the plantations of the Dutch Government in Java.

Formerly the trees were felled close to the ground and stripped of bark, but later the discovery was made that a more profitable yield could be obtained by merely removing the bark in strips

or sections from the standing trees, the decorticated portion being renewed if protected, and as rich in alkaloids as before, and, likewise, that the yield of alkaloids could be materially increased by covering the bark with moss or matting, thereby preventing the rays of the sun from converting these principles into coloring matter. Again, it was found that by careful selection of favorable species, and by crossing and again selecting, barks may be produced that will yield double or even treble the quantity produced by the best non-hybrid varieties. The alkaloids, quinine in particular, are now chiefly extracted from the bark covering the roots, while the bark covering the trunk is employed in the production of the galenical preparations of cinchona.

*Calisaya*, or "yellow," bark is one of the most important varieties, inasmuch as quinine constitutes from one-fourth to three-fourths of its total alkaloidal yield, which makes up about 6 or 7 per cent. of the total weight of the bark. Most of the product, as now met with, is a yellow bark rolled from flat pieces, coming from Bolivia; there are also "quilled" and doubly quilled varieties, of variable thickness, from 3 inches to 2 feet long,  $\frac{1}{4}$  to  $2\frac{1}{2}$  inches in diameter, and  $\frac{1}{12}$  to  $\frac{1}{8}$  inch thick, with a longitudinally wrinkled and transversely fissured, brown epidermis, the latter practically tasteless and inert, and easily separated from the inner, or medicinal, portion. The bark is of short, fibrous texture, compact, presenting shining points wherever broken, of brownish-yellow hue, faint odor, and bitter, slightly astringent taste.

*Red bark* has many alkaloids, but does not yield as much quinine as the calisaya, cinchonidine being present in larger amount. It comes in quills and

flat pieces, varying in thickness from  $\frac{1}{8}$  to  $\frac{1}{4}$  inch; is of deep-brown or red-brown color, and gives a short, smooth fracture. The epidermis is covered with ridges and often with grayish lichens; but transverse fissures are few. The inner surface is rather coarsely striated. It yields a powder of a deep red-brown hue that is slightly odorous, but astringent and bitter.

The *pale*, or *Lora*, bark, obtained from *C. officinalis*, is grown in many scattered plantations. It yields about 1 to 4 per cent. of total alkaloids, of which 50 to 65 per cent. consists of quinine, and presents a rough exterior surface, grayish in color.

The several varieties of *gray bark*, as obtained uncultivated from South America, yield less than 3 per cent. of alkaloids,—often but 1.5 per cent.,—of which quinine constitutes only 0.3 to 0.6 per cent. The outer surface is whitish or of a clear silvery gray, while the inner varies from yellow to cinnamon-brown.

*Columbian*, or *Carthagena*, bark, varies materially in its yield of alkaloids. *Pitayo* bark contains from 1.5 to 1.8 per cent. of quinine, and is especially rich in quinidine.

The *Cuprea* barks, obtained from the trees of the genus *Remijia*, are not true cinchona barks, but are of interest as being a source of the cinchona alkaloids, with the exception of cinchonidine, which they never contain. The total of alkaloids amounts to 2 to 6 per cent. The barks themselves are of a copper-red color, are hard, and contain, in addition to the usual cinchona alkaloids, caffeic acid and quinine caffeine.

According to Gane and Webster, almost all the bark of commerce at present is from hybrid species of cinchona, and the demand for special varieties

is steadily diminishing. Tunmann in 1910 estimated the yearly production of cinchona bark at 10 million kilograms and that of quinine at 500,000 kilograms.

**CONSTITUENTS OF CINCHONA.**—Many alkaloids are present in cinchona. Their aggregate amount may constitute as much as 11 per cent. of the weight of the bark. The most important are *quinine*, *quinidine*, *cinchonine*, and *cinchonidine*. Solutions of the first and last of these are levogyre, while those of quinidine and cinchonine induce dextrorotation. Quinine and quinidine are isomeric, both having the molecular formula  $C_{20}H_{24}O_2N_2$ , while cinchonine and cinchonidine are similarly both expressed as  $C_{19}H_{22}O_2N_2$ . Other alkaloids that have been isolated from cinchona include quinamine, quinamidine, conquinamine, hydroquinine, hydroquinidine, hydrocinchonidine, homocinchonidine, cusconine, cuscamine, quairamine, etc. In addition to these basic substances, there occur in cinchona *kinic* or *quinic acid*, a substance allied to benzoic acid, present to the extent of 5 to 9 per cent., found also in the coffee bean and yielding, in combination with quinine, quinine quinate; *kinorin*, or *quinorin*, a bitter glucosid; *quinovic acid*; *cinchotannic acid*, the astringent constituent of cinchona, which yields a green color when brought in contact with ferric salts; *cinchona red*, a red, almost insoluble glucosid, derived from cinchotannic acid through the action of an oxidizing ferment, and responsible for the color of the red bark; crystalline *calcium oxalate*; starch; gum; wax; resin; an odoriferous volatile oil, in minute amount, and a small percentage of ash.

The alkaloids are extracted from the bark by mixing it with milk of lime,

after grinding it, evaporating to dryness, extracting the resulting mass with chloroform or petroleum, and shaking the extract with dilute sulphuric acid, whereby the alkaloids are dissolved out as sulphates. Upon neutralization and concentration of the resulting solution, the alkaloidal salts crystallize out, quinine sulphate appearing first. After all the alkaloids capable of crystallizing have done so, further evaporation results in the formation of a brown extract containing certain amorphous alkaloids, and termed *quinoidine*.

Quinine, when distilled with potash, yields *quinoline*. Its salts, all extremely bitter, exhibit a characteristic fluorescence in dilute aqueous solutions, which, however, disappears when either a chloride, bromide, or iodide is added.

#### PREPARATIONS AND DOSES.

—The official preparations derived from cinchona are as follows:—

**A. Alkaloidal.** *Quinina* (quinine), a bulky, white, crystalline or amorphous powder, with a very bitter taste; practically insoluble in water (1550 parts), but dissolving, when crystalline, in 0.6 parts of alcohol, 1.3 of ether, 1.6 of chloroform, and 212 of glycerin. Dose, 1 to 30 grains (0.06 to 2 Gm.); official average dose, 4 grains (0.25 Gm.).

*Quinina bisulphas* (quinine bisulphate or acid sulphate of quinine;  $C_{20}H_{24}N_2O_2 \cdot H_2SO_4 + 7H_2O$ , containing 58.12 per cent. of pure quinine), occurring in colorless crystals, which effloresce and become opaque on exposure to the air; soluble in 8.5 parts of water, 18 of alcohol, and 18 of glycerin, but practically insoluble in ether or chloroform. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Quinina dihydrochloridum* (quinine dihydrochloride or acid hydrochloride;

quinine bimuriate) [ $C_{20}H_{24}O_2N_2 \cdot 2HCl$ ], occurring as a white powder; soluble in about 0.6 parts of water and in 12 parts of alcohol at 25° C., slightly soluble in chloroform and very slightly soluble in ether. Its aqueous solution is strongly acid to litmus. Dose, tonic,  $1\frac{1}{2}$  grains (0.1 Gm.); anti-malarial, at least 15 grains (1 Gm.) a day.

*Quinina et urea hydrochloridum* (quinine and urea hydrochloride) [ $C_{20}H_{24}O_2N_2 \cdot HCl \cdot CO(NH_2)_2 \cdot HCl + 5H_2O$ ], a compound of the hydrochlorides of quinine and urea, containing not less than 58 per cent. of alkaloidal quinine. Occurs in colorless, translucent prisms or as a white granular powder; soluble in 0.9 part of water and in 2.4 parts of alcohol at 25° C., soluble in about 800 parts of chloroform. Concentrated solutions in water are straw-colored, slightly viscid, and acid in reaction. Dose, 1 to 30 grains (0.06 to 2 Gm.); hypodermic dose, 15 grains (1 Gm.).

*Quinina hydrobromidum* (quinine hydrobromide;  $C_{20}H_{24}N_2O_2 \cdot HBr + H_2O$ ), occurring in white, silky needles, which are soluble in 40 parts of water at 25° C., 3 of water at 80° C., 0.67 of alcohol, 8 of glycerin, and 16 of ether, and dissolve very readily in chloroform. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Quinina hydrochloridum* (quinine hydrochloride or muriate;  $C_{20}H_{24}N_2O_2 \cdot HCl + 2H_2O$ ), occurring in white, silky needles; soluble in 18 parts of water at 25° C., 0.4 of water at 80° C., 0.6 of alcohol, 8 of glycerin, 240 of ether, and 0.8 of chloroform. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Quinina salicylas* (quinine salicylate;  $2C_{20}H_{24}N_2O_2 \cdot C_7H_6O_3 + H_2O$ ), occurring in fine, white crystals; soluble in 77

parts of water at 25° C., 35 of water at 80° C., 11 of alcohol, 16 of glycerin, 110 of ether, and 37 of chloroform. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Quinina sulphas* (quinine sulphate; neutral quinine sulphate;  $[(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 + 7H_2O]$ ), occurring as white, shining, easily compressible needles, which absorb moisture from damp air and darken on exposure to light; soluble only in 720 parts of water at 25° C. and in 45 at 80° C., in 86 of alcohol, 36 of glycerin, and 400 of chloroform; almost insoluble in ether; easily soluble in dilute acids and in a mixture of 2 parts of chloroform and 1 of absolute alcohol. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Quinina tannas* (quinine tannate), a compound of quinine with tannic acid, of somewhat varying composition and containing not less than 30 nor more than 35 per cent. of alkaloidal quinine. Occurs as a pale-yellow, or yellowish-white, amorphous powder, odorless, and almost or quite tasteless and non-astringent; fairly soluble in alcohol, but only slightly soluble in water, chloroform, and ether. Dose, 2 to 45 grains (0.12 to 3 Gm.). Should be preserved in well-closed containers, protected from light. A useful preparation for children, because of its tastelessness, though its insolubility detracts from its certainty of action.

*Cinchonina sulphas* (cinchonine sulphate; neutral cinchonine sulphate), occurring as colorless, very bitter crystals; soluble in 58 parts of water, 10 of alcohol, and 69 of chloroform, and insoluble in ether. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Cinchonidina sulphas* (cinchonidine sulphate; neutral cinchonidine sul-

phate), occurring in white, silky crystals, which effloresce on exposure to air; soluble in 63 parts of water, 72 of alcohol, and 900 of chloroform, and insoluble in ether. Dose, 1 to 30 grains (0.06 to 2 Gm.); average, 4 grains (0.25 Gm.).

*Ferri et quinina citras* (soluble iron and quinine citrate; quinine ferro-citrate with ammonia), containing not less than 13 per cent. of iron and 11.5 per cent. of quinine. Occurs as greenish or golden-yellow, deliquescent scales; rapidly and completely soluble in water as well as in dilute alcohol. Dose, 3 to 10 grains (0.2 to 0.6 Gm.).

**B. Crude Drug.** *Cinchona* (bark of *Cinchona ledgeriana*, *C. calisaya*, and *C. officinalis*). It is required to contain at least 5 per cent. of total alkaloids and 4 per cent. of anhydrous ether-soluble alkaloids. Dose, 15 grains (1 Gm.).

*Cinchona rubra* (bark of *Cinchona succirubra*). It is required to contain at least 5 per cent. of alkaloids. Dose, 15 grains (1 Gm.).

*Fluidextractum cinchonæ* (fluidextract of cinchona). Contains 5 per cent. of alkaloids. Dose, 15 minims (1 c.c.).

*Tinctura cinchonæ* (tincture of cinchona). *Calisaya cinchona*: 20 per cent. Dose, 1 fluidram (4 c.c.).

*Tinctura cinchonæ composita* (compound tincture of cinchona; Huxham's tincture). Red cinchona, 10 per cent.; bitter orange, 8 per cent.; serpentaria, 2 per cent. Dose, 1 fluidram (4 c.c.).

The following preparations derived from cinchona are semi-official, being mentioned in the National Formulary (N. F. IV):—

*Vinum ferri amarum*, N. F. (bitter wine of iron), containing 5 per cent. of soluble iron and quinine citrate. Dose, 2 fluidrams (8 c.c.).

*Elixir ferri, quininae, et strychninae*, N. F. (elixir of iron, quinine, and strychnine). In effect a solution of tincture of ferric citro-chloride, 12.5; quinine hydrochloride, 0.875, and strychnine sulphate, 0.0175, in aromatic elixir, to make 100. Dose, 1 fluidram (4 c.c.).

*Syrupus ferri, quininae, et strychninae phosphatum*, N. F. (syrup of iron, quinine, and strychnine phosphates). Dose, 1 fluidram (4 c.c.), containing about  $1\frac{1}{4}$  grains (0.08 Gm.) of ferric phosphate,  $1\frac{1}{2}$  grains (0.1 Gm.) of quinine together with  $\frac{1}{80}$  grain (0.0008 Gm.) of strychnine.

*Syrupus hypophosphitum compositus* N. F. (comp. syrup of hypophosphites). Contains, in addition to a mixture of calcium, sodium, potassium, iron, and manganese hypophosphites, 0.11 per cent. of quinine, 0.011 per cent. of strychnine, 0.375 per cent. of sodium citrate, and 1.5 per cent. of dilute hypophosphorous acid. Dose, 2 fluidrams (8 c.c.).

*Oleatum quininae*, N. F. (oleate of quinine). Contains 25 per cent. of quinine.

*Tinctura antiperiodica* (N.F.) (Warburg's tincture). Contains in each fluidounce (30 c.c.) 10 grains (0.6 Gm.) of quinine sulphate;  $3\frac{1}{2}$  grains (0.23 Gm.) each of rhubarb and angelica seed;  $1\frac{3}{4}$  grains (0.12 Gm.) each of elecampane, saffron, and fennel, and  $\frac{7}{8}$  grain (0.06 Gm.) each of aqueous extract of aloes, gentian, zedoary, cubeb, myrrh, white agaric, and camphor. The preparation is sometimes ordered "without aloes." Dose, 4 fluidrams (16 c.c.).

*Pilula antiperiodica* (N.F.) (Warburg's pill). Each pill contains  $1\frac{1}{2}$  grains (0.085 Gm.) of quinine sulphate; 1 grain (0.06 Gm.) of aqueous extract

of aloes;  $\frac{1}{2}$  grain (0.03 Gm.) of rhubarb;  $\frac{1}{4}$  grain (0.015 Gm.) each of elecampane, saffron, and fennel;  $\frac{1}{8}$  grain (0.008 Gm.) each of zedoary, cubeb, myrrh, white agaric, and camphor, and extract of gentian, a sufficient quantity. Like the tincture, these pills may be ordered "without aloes." Dose, 2 pills.

*Elixir ferri pyrophosphatis, quininae, et strychninae* (N. F.). A solution of ferric pyrophosphate, 3.5, in distilled water with aromatic elixir, to make 100. Dose, 1 fluidram (4 c.c.).

*Elixir quininae et phosphatum compositum* (N. F., III). Each  $\frac{1}{4}$  fluidounce (8 c.c.) represents  $\frac{1}{2}$  grain (0.03 Gm.) of quinine sulphate,  $1\frac{1}{2}$  grains (0.1 Gm.) of calcium lactophosphate, and 2 grains (0.12 Gm.) of soluble ferric phosphate. Dose, 2 fluidrams (8 c.c.).

*Elixir quininae valeratis et strychninae* (N. F.). A solution of quinine valerate, 1.75, and strychnine sulphate, 0.0175, in a mixture of compound tincture of cudbear, distilled water, and aromatic elixir, to make 100. Dose, 1 fluidram (4 c.c.).

*Mistura splenetica* (N. F., III) (Gadberry's mixture). Each fluidram (4 c.c.) represents about 2 grains (0.12 Gm.) of quinine sulphate, 1 grain (0.06 Gm.) each of potassium nitrate and ferrous sulphate, and 1 minim (0.06 c.c.) of nitric acid. Dose, 1 fluidram (4 c.c.).

*Tinctura cinchonae detannata* (N. F., III). Represents the official tincture from which the tannin has been removed by means of iron. Has been used for the preparation of elixirs of cinchona containing iron salts.

*Elixir cinchonae alkaloidorum*, (N. F.). Two fluidrams contains  $\frac{1}{4}$  grain (0.015 Gm.) of quinine sulphate and  $\frac{1}{8}$

grain (0.008 Gm.) each of sulphates of cinchonine and cinchonidine, in aromatic elixir. Dose, 2 fluidrams (8 c.c.).

*Elixir cinchonæ alkaloidorum et ferri* (N. F.). The preceding with admixture in each  $\frac{1}{4}$  fluidounce (8 c.c.) of 4 grains (0.25 Gm.) of soluble ferric phosphate. Dose, 2 fluidrams (8 c.c.).

*Elixir cinchonæ alkaloidorum, ferri, et bismuthi* (N. F.). A mixture of glycerite of bismuth, 6.5, with distilled water and the preceding preparation, to make 100. Dose, 2 fluidrams (8 c.c.).

*Elixir cinchonæ alkaloidorum, ferri, bismuthi et strychninæ* (N. F.). Dose, 1 fluidram (4 c.c.).

*Elixir cinchonæ alkaloidorum, ferri, et calcii lactophosphatis* (N. F.). Dose, 2 fluidrams (8 c.c.).

*Elixir cinchonæ alkaloidorum, ferri, et pepsini* (N. F.). Dose, 2 fluidrams (8 c.c.).

*Elixir cinchonæ alkaloidorum, ferri, et strychninæ* (N. F.). Dose, 1 fluidram (4 c.c.).

*Elixir cinchonæ alkaloidorum et hypophosphitum* (N. F.). Dose, 2 fluidrams (8 c.c.).

*Elixir cinchonæ, pepsini, et strychninæ* (N. F., III). Each fluidram (4 c.c.) represents  $\frac{1}{100}$  grain (0.0006 Gm.) of strychnine sulphate and 1 grain (0.06 Gm.) of pepsin. Dose, 1 fluidram (4 c.c.).

*Elixir ammonii valerianatis et quinina* (N. F., III). Each fluidram represents  $\frac{1}{4}$  grain (0.015 Gm.) of quinine hydrochloride and 2 grains (0.12 Gm.) of ammonium valerate. Dose, 1 or 2 fluidrams (4 or 8 c.c.).

*Syrupus phosphatum cum quinina et strychnina* (N. F.). A solution of quinine hydrochloride, 0.44, strychnine nitrate, 0.014, in a mixture of compound solution of phosphates, 50, glyc-

erin, 15, and syrup, to make 100. Dose, 1 fluidram (4 c.c.).

*Pilulæ ferri, quinina, aloes, et nucis vomica* (N. F.). Each contains exsiccated ferrous sulphate, 0.065, quinine sulphate, 0.065, aloes, 0.065, extract of nux vomica, 0.016, and extract of gentian, to make a mass. Dose, 1 pill.

*Pilulæ ferri, quinina, strychnina, et arseni fortiores* (N. F.). Each contains reduced iron, 0.065, quinine sulphate, 0.065, strychnine, 0.0032, and arsenic trioxide, 0.0032. Dose, 1 pill.

*Pilulæ ferri, quinina, strychnina, et arseni mites* (N. F.). Each contains reduced iron, 0.045, quinine sulphate, 0.065, strychnine, 0.0013, and arsenic trioxide, 0.0013. Dose, 1 pill.

Among the unofficial preparations containing cinchona alkaloids or allied to them are the following:—

*Quinine hydrochlorosulphate* (quinine sulphochloride)  $[(C_{20}H_{24}N_2O_2)_2 \cdot HCl \cdot H_2SO_4 + 3H_2O]$ , containing 74 per cent. of quinine. Occurs in fine, white needles; soluble in an equal amount of water and in alcohol. Dose, 1 to 30 grains (0.06 to 2 Gm.). Suitable for hypodermic use.

*Quinine formate*  $[C_{20}H_{24}N_2O_2 \cdot HCOOH]$ , containing about 85 per cent. of quinine. Occurs in white crystals; easily soluble in water and in alcohol. Dose, 1 to 30 grains (0.06 to 2 Gm.). Suitable for hypodermic use.

*Quinine lactate*  $[C_{20}H_{24}N_2O_2 \cdot CH_3 \cdot CH(OH) \cdot COOH]$ , containing 78 per cent. of quinine. Occurs in white crystals; soluble in 10 parts of water and in alcohol. Dose, 1 to 30 grains (0.06 to 2 Gm.). Suitable for hypodermic use.

*Quinine valerate* (quinine valerianate)  $[C_{20}H_{24}N_2O_2 \cdot (CH_3)_2 \cdot CH \cdot CH_2 \cdot COOH + H_2O]$ , containing 73 per cent. of quinine. Occurs in colorless crystals or powder, having a slight odor



of valerian; soluble in 100 parts of water and in 5 parts of alcohol. Dose, 1 to 30 grains (0.06 to 2 Gm.).

*Quinine ethyl carbonate* (euquinine) [ $C_2H_5O.COOC_20H_{23}N_2O$ ], containing 82 per cent. of quinine. Occurs as a light, fleecy, white powder of crystalline needles; practically tasteless; easily soluble in alcohol, chloroform, and ether, but only slightly soluble in water. If it is dissolved in acidulated water, the bitter quinine taste is unmasked. Dose, 1 to 30 grains (0.06 to 2 Gm.). Useful for children, but acts more slowly than the soluble quinine salts. Its decomposition in the alimentary canal is more steady and certain than in the case of the tannate (Sollmann).

*Diquinine carbonate* (aristochin; neutral quinine carbonic acid ester) [ $C_{20}H_{23}N_2O.O.COOC_{20}H_{23}N_2O$ ], containing 96.1 per cent. of quinine. Occurs as a white, tasteless powder; insoluble in water, with difficulty soluble in alcohol and chloroform, and almost insoluble in ether. In acid preparations it is slowly decomposed, with liberation of quinine. Dose, 1 to 30 grains (0.06 to 2 Gm.).

*Phenetidin quinine carbonate* (chinaphenin; phenetidin quinine carbonic acid ester) [ $C_2H_5O.C_6H_4.NH.COOC_{20}H_{23}N_2O$ ]. Occurs as a white, tasteless powder; soluble with difficulty in water, but easily soluble in alcohol, chloroform, and ether. Quinine is liberated from it in acid solutions. Dose, 1 to 30 grains (0.06 to 2 Gm.). Combines the effects of quinine and acetphenetidin.

*Quinine salicylic ester* (saloquinine; salicylquinine; quinine salicylic acid ester) [ $C_6H_4.OH.COOC_{20}H_{23}N_2O$ ], containing 73.1 per cent. of quinine. Occurs as a white, tasteless, crystalline powder; insoluble in water, but moderately soluble in alcohol and ether, and

more easily soluble in acidulated water. Dose, 1 to 30 grains (0.06 to 2 Gm.).

*Saloquinine salicylate* (salicylate of quinine salicylic acid ester) [ $C_6H_4.OH.COOC_{20}H_{23}N_2O.C_6H_4.OH.COOH$ ]. Occurs as a white, tasteless, crystalline powder; slightly soluble in water, and soluble in hot alcohol and in chloroform. It is incompatible with alkalis. Dose, 1 to 30 grains (0.06 to 2 Gm.).

*Quinine lygosinate* (quinine salt of dioxydibenzylacetone) [ $CO(CH:CH.C_6H_4.OH.C_{20}H_{24}N_2O_2)_2$ ], a condensation product of salicylic aldehyde and acetone, containing about 70 per cent. of quinine. Occurs as an amorphous, orange-yellow powder, with a slight aromatic odor and slowly developing bitter taste. It is slightly soluble in water, easily soluble in alcohol, chloroform, and benzene, and fairly soluble in hot oil. Acids and alkalis decompose it. Employed externally as dusting powder, in glycerin suspension, on gauze, and in suppositories.

*Quinctum* (chinetum; cinchona febrifuge), a mixture of the alkaloids occurring in red cinchona bark, devised by East Indian authorities as a cheaper and safer remedy than quinine. Occurs as an amorphous, grayish-white or brownish powder, containing from 50 to 70 per cent. of cinchonidine. It is slightly soluble in water, more easily in dilute acids. Dose, 1 to 30 grains (0.06 to 2 Gm.). A more soluble neutral sulphate of quinctum is also available.

*Quinoidine* (chinoidine), a mixture of the amorphous alkaloids remaining in solution after the crystalline alkaloids in the chloroform or petroleum extract from cinchona bark have been removed. Occurs as a very bitter, brownish-black mass, lustrous and resinous in appearance; soluble in dilute acids, alcohol, and chloroform. Dose, 1 to 15 grains (0.06 to

1 Gm.). Soluble salts of quinoidine, such as the borate, citrate, hydrochloride, and sulphate, may be used instead.

Basic quinine acetylsalicylate is prepared by mixing equimolecular amounts of acetylsalicylic acid and quinine hydrate and dissolving them in ether; an oily precipitate forms, which soon becomes a crystalline mass. The substance is a bitter, white salt, slightly soluble in water, more soluble in alcohol and chloroform, and almost insoluble in ether. Trials seem to show that this salt is of value in pleurisy and peritonitis, and that it is a more effective antipyretic than the ordinary quinine salts. The ordinary dose is 6 grains (0.4 Gm.). Santi (*Les nouveaux remèdes*, vol. xxiii, No. 5, 1907).

Treatment to insure cure must destroy every parasite. Disappearance of clinical symptoms and of parasites from the peripheral circulation cannot be depended on. The duration of proper quinine treatment is the only reliable guide. To be practical, it must be convenient and not produce great discomfort. Unusual salts of quinine are objectionable, the best of all being the sulphate. One dose of 10 grains (0.6 Gm.) of quinine sulphate daily for a period of 8 weeks disinfected more than 90 per cent. of cases of malaria in the large area of Louisiana under observation. C. C. Bass (*Trans. Amer. Med. Assoc.*, June 12, 1919).

#### MODES OF ADMINISTRATION.

**Oral.**—The chief difficulty attending the administration of quinine by the mouth is its bitter taste. Where small doses are to be given, and rapidity of action is not essential, this difficulty may be overcome without great disadvantage either by administering the drug in capsules, in cachets, or in pills coated with gelatin, sugar, or chocolate (preference being given to quinine bisulphate or hydrochloride as acting the most rapidly when once liberated),

or, again, by using practically insoluble preparations, such as the uncombined alkaloid quinine or quinine tannate, which do not reach the peripheral taste-organs in sufficient amount to provoke a bitter sensation.

The insoluble preparations act with great slowness and are somewhat uncertain in effect, since they must be rendered soluble by combination with the hydrochloric acid of the gastric juice before ready absorption can occur. It is therefore recommended that their ingestion be followed by that of dilute hydrochloric acid, *e.g.*, in lemonade, in order to hasten their dissolution.

Where coated pills are employed, the gelatin coating should be thin and the sugar or chocolate not hardened by age. In the case of capsules or cachets, which are always preferable to pills, the more soluble salts of quinine should, as a rule, be used. Although the official hydrochloride, which dissolves in 18 parts of water, and the bisulphate, soluble in 8.5 parts, are far superior to the sulphate in rapidity of action, the latter, which is soluble only in about 700 parts, has been considerably employed in the past, and this may be said in its favor, *viz.*, that slow absorption involves a more prolonged, if less intense, effect,—a feature which may at times be of advantage.

The hydrochloride contains 82 per cent. of alkaloidal quinine, as compared to 73 per cent. in the case of the sulphate and 59 per cent. in the bisulphate; this difference in its favor is, however, of no great significance, since a mere readjustment of dosage is all that is required to render the three salts equivalent. The official hydrobromide is another salt that is fairly soluble, and may prove useful where combined quinic and sedative effects are desired.

The bisulphate of quinine was introduced on account of its greater solubility as compared with the ordinary sulphate. But it carries a large quantity of sulphuric acid into the stomach and so causes indigestion. The bihydrochloride is the best salt of quinine for internal administration. B. Howard (Chemist and Druggist, March 23, 1907).

Where some bitterness of taste is not objectionable, any of the quinine salts may be given in, *e.g.*, a dessertspoonful of syrup of orange, in syrup of wild cherry, or in a little whisky and water. Jacobi suggests that the quinine be mixed in a tablespoon with cold, strong black coffee. Again, by rubbing up quinine with one-fourth its weight of ammoniated glycyrrhizin (official as *glycyrrhizinum ammoniatum*) its bitter taste can be largely disguised.

If rapidity and reliability of action are of great importance, however, the drug should by preference be administered in solution. Particularly is this true where large doses are to be given. In the case of quinine sulphate, the amount of fluid present in the stomach is not likely to be sufficient to dissolve immediately large doses given in dry form, and a large proportion of the drug may even remain entirely unabsorbed.

Quinine sulphate may be rendered more soluble by the addition of dilute sulphuric acid, and is frequently thus dispensed when ordered in aqueous solution, since the 700 parts of water required for dissolution would result in a product far too bulky for convenience. The amount of acid included should be at least one drop for each grain of quinine, for unless an excess be present some of the alkaloid may be precipitated on the tongue through the alkalinity of the saliva, a prolonged

bitter after-taste resulting. The immediate taste, however, is by this method rendered more pronounced than would be the case with unmodified quinine sulphate. It is therefore often preferable either to use strong flavoring agents, especially licorice, or to give the drug merely in a state of suspension in some syrupy preparation. This may be done either with the sulphate or with the other salts. Thus, one might prescribe:—

R *Quinina sulphatis* .. ʒj (4 Gm.).  
*Fluidextracti glycyrrhizæ* ..... fʒss (15 Gm.).  
*Elixiris aromatici*,  
 q. s. ad ..... fʒiij (100 Gm.).

M. Sig.: Shake before using.

Or,

R *Quinina hydrochloridi* ..... ʒj (4 Gm.).  
*Syrupi glycyrrhizæ*,  
 q. s. ad ..... fʒiij (100 Gm.).

M. Sig.: Shake before using.

Other preparations containing licorice which may be used are the *elixir glycyrrhizæ* (U. S. P.), containing 12 per cent. of licorice; *glycyrrhizinum ammoniatum* (U. S. P.), an active substance from licorice combined with ammonia for solubility; *elixir glycyrrhizæ aquosum* (N. F.), and *elixir glycyrrhizæ aromaticum* (N. F.), a combination of licorice with oils of cloves, cinnamon, nutmeg, and fennel. To no preparation containing licorice is it permissible to add acid for the purpose of rendering quinine soluble, as the glycyrrhizin would thereby be precipitated.

Eriodictyon (*yerba santa*) is also useful to overcome the bitter taste of quinine. It tends to paralyze the peripheral organs somewhat as does cocaine, but destroys only bitter tastes and exerts no constitutional effect. It is official in *Fluidextractum eriodictyi*,

dose 10 to 30 minims (0.6 to 2 c.c.), and semiofficial in *Elixir eriodictyi aromaticum* (N. F.), dose 1 to 2 fluidrams (4 to 8 c.c.).

A sluggish liver and constipation both detract from the action of quinine, and in such cases some cathartic such as mercury or euonymus should be given with it. Likewise, where there is gastric irritability, as in alcoholics, it should be combined with calomel in the proportion of  $1\frac{1}{2}$  grains (0.1 Gm.) of quinine to 1 grain (0.65 Gm.) of calomel (Beard).

Vomiting from quinine can easily be prevented by giving the drug four or five hours after food or at an interval of two hours before food, in solution if possible, so that it may be easily and rapidly absorbed. Calomel and Seidlitz powders once in a while are of advantage. A. M. Mudaliar (The Antiseptic, Oct., 1909).

In children, small capsules may be used, if the little patients be not too young. Quinine chocolates, each containing 1 grain (0.06 Gm.) of the tannate, which is practically tasteless, also constitute an eligible preparation, though the tannate is the least active salt of the alkaloid. Where the tannate is not available it can be prepared extemporaneously by either of the following formulæ:—

℞ *Quinina* ..... gr. xxiv (1.5 Gm.).  
*Acidi tannici* .. gr. xij (0.75 Gm.).  
*Syrupi cinna-*  
*moni* (N. F.). f̄ij (100 Gm.).—M.

Or,

℞ *Quinina hydro-*  
*chloridi* ..... gr. xxiv (1.5 Gm.).  
*Acidi tannici*,  
*Glycyrrhizini*  
*ammoniat*i .āā gr. xij (0.75 Gm.).

M. et div. in pulv. no. xij.

Quinine ethyl carbonate (euquinine), which is practically tasteless, may also

be used in children. Its taste disappears entirely if it is given suspended in sweetened milk. Its relative insolubility, however, implies the same slowness of action as obtains with the tannate, though the percentage of alkaloidal quinine it contains is about  $2\frac{1}{2}$  times as great as that of the latter compound.

As a fluid preparation of quinine for children, Hare suggests the following:—

℞ *Quinina hydrochlo-*  
*ridi* ..... gr. xvj (1 Gm.).  
*Fluidextracti glycyrrhizæ* ..... f̄ij (4 Gm.).  
*Syrupi aurantii* .... f̄ij (60 Gm.).

M. Sig.: One teaspoonful three times daily for a child of 3 years.

Comby recommends:—

℞ *Quinina hydro-*  
*chloridi* ..... gr. xxx (2 Gm.).  
*Benzosulphinidi* ... gr. v (0.3 Gm.).  
*Tinctura aurantii*  
*amari* ..... m̄lxx (5 Gm.).  
*Syrupi* ..... f̄ij (60 Gm.).—M.

Bordes administers quinine with olive oil. Fifteen grains (1 Gm.) of the sulphate are mixed with 120 grains (8 Gm.) of olive oil in a mortar. The required number of drops is placed in a tablespoon half-filled with milk and sugar. The quinine being enclosed in oil, which floats at the surface, the whole slips down easily, and is followed by a little water or milk. Quinine may also be given in 3 parts of melted cacao butter, which is administered in a spoonful of warm milk.

The following quinine mixture recommended as especially palatable and consequently useful in administering the drug to children: From 5 to 10 grains (0.32 to 0.65 Gm.) of quinine are dissolved in a dram (4 Gm.) of alcohol. From 30 to 40 minims (1.85 to 2.5 c.c.) each of oil of cinnamon and oil of anise are then mixed

with a small quantity of magnesia and an ounce (30 c.c.) of water. After permitting this to stand some hours it is filtered. The two mixtures are then combined and added to 3 ounces (45 c.c.) of simple syrup with 5 drops (0.3 c.c.) of carmine or cochineal solution. The dose is from 1 to 2 drams (4 to 8 Gm.). Sodium bromide or small doses of Fowler's solution may be added if desired. Greanellé (*N. Y. Med. Jour.*, Oct. 28, 1899).

**Rectal.**—This method should be resorted to only where the oral route is unavailable. For children the administration in suppositories is especially useful, a few grains of quinine hydrochloride being given in, say, 15 or 30 grains of cacao butter. In adults 10 to 25 grains (0.6 to 1.6 Gm.) of the drug may be incorporated in 60 to 90 grains (4 to 6 Gm.) of the excipient. Administration by enema, in 2 to 6 ounces (60 to 200 Gm.) of water, to which may be added 10 grains (0.6 Gm.) of antipyrin, or 10 minims of laudanum, is also practicable. The amount given by the rectum should be about double that used by the mouth.

Either of these procedures is, however, apt to induce irritation of the rectum if its employment is persisted in.

**Cutaneous.**—In infants quinine hydrochloride may be administered by inunction. The ointment used should contain 10 or 20 per cent. of the drug, and be rubbed into the skin of the axillæ morning and evening. The use of the hydrochlorosulphate of quinine, 1 part to 5 of benzoated lard or other base, has been advised.

In administering quinine by inunction the method almost universally employed has been to mix the drug with lard or vaselin and rub the patient with it. There is no doubt but that thousands of helpless children have been slain by the malarial germ

while their physician stood by and credulously depended upon securing the effects of quinine by this impossible method. There is, however, a medium in which some of the salts of quinine may be administered by inunction with perfect success: glycerin. The hydrochloride and bisulphate of quinine are perfectly soluble in warm glycerin in the proportion of 1 part of quinine to 3 parts of glycerin, thus making a 25 per cent. solution. The glycerin has such an affinity for the water of the blood that it passes readily through the integument and carries with it the quinine, which it holds in perfect solution.

In the more severe forms of pernicious malarial diseases, if quinine is administered by the stomach, rectum, or even hypodermically, absorption may be so deranged that it will not be taken up; but so long as the blood is circulating, if one of the soluble salts of quinine be dissolved in glycerin and applied to the skin it will pass into the blood, the skin acting merely as a dialyzing membrane. A patient can be quinized as promptly and as thoroughly in this way as in any other. The method is suitable for either adults or children; but in estimating the dose, allowance should be made for waste because of contact with the clothing before all the compound has been taken up. Gentle friction should be practised for a few minutes after applying the remedy, as this stimulation of the capillary circulation will hasten the taking up of the glycerole. A convenient form of ordering the compound is: Quinine hydrochloride,  $\mathfrak{z}\text{ij}$  (8 Gm.); glycerin (warm),  $\mathfrak{z}\text{vj}$  (24 Gm.). Use 2 drams (8 Gm.) as inunction for an adult. G. E. Pettey (*Memphis Med. Monthly*, July, 1908).

**Hypodermic.**—This method is useful where, the condition present being serious, an immediate, powerful effect is desired, or where the drug is vomited if administered by the mouth, and diarrhea prevents rectal use. The injection

should preferably be given into muscles, *e.g.*, into the glutei, as it is then less painful, acts more rapidly, and is less likely to induce marked local irritation or abscess formation than if given subcutaneously. Scrupulous care should, however, always be taken to secure asepsis in administering the injection, as local sloughing, septicemia, and even tetanus have been known to occur where these precautions were overlooked. The syringe and needle should be sterilized by boiling, and the fluid used boiled for some time both before and after the addition of the quinine.

Experiments performed on relation of quinine injections to tetanus. The drug has not the power to awaken an infection when injected at the same time with the tetanus spores or at other times. In most of the cases in which tetanus has followed quinine injections it can be traced to some fault of surgical technique or to some contamination of the quinine solution. Tissue necrosis from quinine injections would favor infection by tetanus germs as well as by other bacteria. There is not sufficient proof that the tetanus spores can be transported from point to point according as the quinine is injected, nor that it is possible for the healthy living spores of tetanus to be present in the body and to develop a severe and fatal infection on the advent of an injection of hydrochloride of quinine. E. F. McCampbell (Jour. Amer. Med. Assoc., March 16, 1907).

Sloughs following a very superficial subcutaneous injection of quinine can always be avoided if the general condition of the patient is not bad. Abscesses following intramuscular injections occur almost always in patients previously infected or intoxicated. Every such injection should be given slowly, in small doses and at a point not used in previous treatment, in the gluteal or abdominal regions. The patient should remain quiet and limit as far

as possible the number and force of muscular contractions in the region affected during the day following the injection. R. de Gaulejac (La presse méd., May 13, 1908).

The author noticed that in a large number of lean patients to whom subcutaneous injections of the neutral hydrochloride of quinine were given no unpleasant local effects were produced, while in 2 stout patients areas of induration, with necrosis, evacuation of a species of fatty emulsion, and final healing with depressed scars, were produced. He believes that the occasional destructive local effects of quinine are due to the action of the drug on the subcutaneous fatty layer, which, as is well known to surgeons, is of low vitality, and which is likely to be entered by the needle when the skin is lifted up for making the injection. If the changes in the subcutaneous tissues proceed far enough, the nutrition of the overlying skin is involved through destruction of the capillaries and nerve-endings. Such effects do not result from intramuscular injection, because the needle is passed entirely through the fat. The healing of the lesions caused by subcutaneous injections of quinine is hastened by dissection and removal of the disorganized, semiliquid, yellowish masses of fat present under the skin. F. Gorriti (Arch. gén. de méd., Oct., 1909).

It has been shown by Vincent that if an insoluble salt of quinine be injected subcutaneously, and tetanus bacilli be injected soon afterward, these will later be found in greatest abundance at the site of the quinine injection and not at the site of their own entrance. This is believed to be due to the effect of quinine in paralyzing phagocytosis. In most instances there had been either an abscess following the injection or local necrosis of the skin. In giving injections of quinine all possible precautions against infection should be taken. The neutral chloride, which has been shown to possess the power of destroying tetanus spores,

should alone be used. The injections should always be given into the muscles rather than hypodermically. Rigollet (*Presse méd.*, Nov. 6, 1909).

When a solution of quinine is boiled, it undergoes a deleterious change in a very short time. However clear it may be before boiling, it is usually opaque on cooling. Boiling for from one to three minutes is entirely inadequate to sterilize quinine so far as tetanus spores are concerned, Theobald Smith having shown that the spores of some strains of tetanus bacilli resist boiling for as long as from forty to seventy minutes. Experiments on guinea-pigs showed that the deterioration of quinine by boiling is not only chemical, but that it materially impairs its therapeutic efficiency; boiled quinine injected in doses sufficient to kill if the drug was not boiled failed to do so.

Quinine produces some change in the tissues which renders them a favorable site for the growth of the tetanus bacillus. It is not so much that the quinine solution actually contains tetanus bacilli, but rather that it predisposes to infection if the germ is present in the body. Quinine itself acts deleteriously upon the tetanus organism. While tetanus following the injection of quinine is a rare occurrence, this method of quinine administration should not be recommended as a routine measure in cases of malaria. In those localities of tropical countries where tetanus frequently occurs, the author would combine with the quinine a dose of tetanus antitoxin as a safeguard. Sir David Semple (*Indian Med. Gaz.*, Dec., 1911).

The best salts to use for injection are the bihydrochloride or acid hydrochloride (official in U. S. P. IX), the neutral hydrochloride (U. S. P.), the double hydrochloride of quinine and urea, and the hydrobromide. French observers also recommend the formate, which is said to cause no pain when injected subcutaneously.

Hypodermic injections of quinine formate used in doses of 20 cg. ( $3\frac{1}{2}$  grains) to 2 c.c. (32 minims) of water, two injections a day being given. Cessation of malarial attacks was obtained as with quinine hydrochloride in doses of 30 cg. (5 grains). The difference between the two medicaments is that the first causes no pain and leaves no trace of its action locally, while the latter is often very painful and leaves local swellings which persist a long time. G. H. Lemaire (*Revue thérap. des alcaloïdes*, May, 1906).

The bihydrochloride may be given dissolved in only 2 parts of sterile water, though pain is minimized if the dilution be somewhat greater. Laveran advises 1 part of quinine to 5 of water. The dose ranges, with all the salts, from  $1\frac{1}{2}$  to 15 grains (0.1 to 1 Gm.). The injection should be given slowly.

The unpleasant sequelæ of the ordinary solutions of quinine when given under the skin are due to the caustic effect of the solutions. A 0.2 per cent. solution of quinine bihydrochloride in normal saline solution was used with excellent results in a number of cases, including some of severe malarial poisoning. The weakness of the solution necessitates the injection of large quantities, but the only precaution necessary is not to inject more than  $2\frac{1}{2}$  drams (10 Gm.) in one spot. An ordinary hypodermic syringe may be used, and the author has employed the treatment over 3000 times without accident. A further point in its favor is that the saline adds to the antimalarial action of the quinine a tonic and diuretic effect. M. Malafosse (*Semaine méd.*, No. 18, p. 208, 1905).

Technique of injections of acid hydrochloride of quinine described: The needle of a small hypodermic syringe is sterilized by boiling for two to three minutes in a test-tube. The syringe is washed out with 1 in 20 carbolic lotion by drawing up some of the solution into the syringe

three or four times. A small spoon is also placed in the 1 in 20 carbolic solution, to be used to receive the quinine lotion when it is poured out from the bottle previous to changing the syringe. The glass stopper together with the neck and mouth of the bottle are thoroughly cleaned with a sponge dipped in 1 in 20, and the part into which the solution is to be injected is, of course, prepared in the usual way. The dose is 10 minims (0.6 c.c.), equal to 10 grains (0.6 Gm.) of the salt, intramuscularly in the deltoid muscle. Sometimes a slight aching sensation occurs while the solution is being injected, but it passes off immediately. The author has never observed symptoms of cinchonism from this method. Symons (*Indian Med. Gaz.*, May, 1907).

The hydrochloride presents, according to Bluenchen, the advantage, together with fairly high solubility (1 in 18), of not crystallizing out when a hot fluid in which it has been dissolved is cooled to body temperature. The following solutions of this salt have been recommended for hypodermic use: (1) Quinine hydrochloride, 7 grains (0.5 Gm.); glycerin and water, of each,  $\frac{1}{2}$  dram (2 c.c.); the solution should be warmed before use, and no acid should be added. (2) Quinine hydrochloride, 15 grains (1 Gm.); alcohol, 15 minims (1 c.c.); distilled water,  $1\frac{1}{2}$  drams (6 c.c.); a few drops of hydrochloric acid are to be added before use to complete the solution.

Not till the strength of a solution of the neutral hydrochloride of quinine is reduced to 3 grains (0.2 Gm.) per 17 minims (1.06 c.c.) can one be sure of avoiding local reaction. This was well shown in cases where the same amount of quinine was injected into the two flanks at the same time, but in different strengths; the strong solution caused abscess, while the weak solution only caused slight redness. The injection must also be

done gently. Slight friction, dispersing the fluid, aids absorption and diminishes the irritating effect. Friction is especially indicated in collapsed cases where the circulation is weak and absorption slow. The least susceptible parts are those where the subcutaneous tissue is most abundant, and, at the same time, least dense, the most suitable places being the gluteal regions and the external surface of the thighs; then the external surface of the arms and the dorsolumbar region. The deeper the injection, the less frequent and less severe the results. When deep injections cause irritation, it is due either to too rapid injection or to the fluid being reflected to the surface from dense tissue underneath. Dilution does not diminish the efficacy of the quinine. Lafforgue (*Gaz. d. hôp.*, Paris, Nov. 14 and 19, 1901).

Injections of quinine should be intramuscular, not subcutaneous. The gluteal, scapular, and deltoid muscles are the ones best suited. The salt of quinine to be used is the hydrochloride, and, of this, 6 grains (0.39 Gm.) are to be dissolved in 40 minims ( $1\frac{1}{4}$  ounces) of boiled water; the solution is brought to the boiling point and allowed to cool. After the injection, which is always painful, the area should be painted with iodine liniment [a preparation similar to Lugol's solution]. Following this method, the author has never seen any untoward occurrences. Injections are probably not absolutely safe in patients suffering from any form of acute septic ulceration, as in these there is a possibility of the area of injection being infected from within. J. P. Maxwell (*Jour. of Tropical Med.*, Feb., 1902).

Quinine given by hypodermic injection in 18 cases. The most suitable preparation is the acid hydrochloride, which is readily soluble in warm distilled water, 1 minim (0.06 c.c.) taking up 1 grain (0.065 Gm.) of quinine. This preparation was found non-irritating and was injected



deeply into the structures below the ribs on the left side, thus getting near to the spleen. The amount given was usually 8 grains (0.5 Gm.), but in severe cases 16 grains (1 Gm.) were given without any bad effects. The results in almost every case were striking, and where no reaction followed the injection it was found that the patient was suffering from some disease other than malaria. There was no headache, no tinnitus, and the disease was cut short; rarely were more than two injections required. C. M. Fleury (Jour. Royal Army Med. Corps, Oct., 1904).

Gaglia and others have recommended the addition of urethane (*æthylis carbamas*) to the hydrochloride or the hydrobromide, both to increase their solubility and avoid irritation. Fifteen grains (1 Gm.) of the quinine salt and  $7\frac{1}{2}$  grains (0.5 Gm.) of urethane can be dissolved in 15 minims (1 c.c.) of warm water. About 30 minims (2 c.c.) of a solution which is permanent, does not precipitate on cooling, and causes no local irritation, are thus obtained. Another method of using the hydrochloride is that of Von Stoffella, who dissolves 30 grains (2 Gm.) of the salt in  $2\frac{1}{2}$  drams (10 c.c.) of distilled water with the aid of heat; upon cooling, the solution becomes a rather firm mass, but this readily liquefies on being warmed before use.

Triulzi pointed out the utility of antipyrin as an agent greatly increasing the solubility of quinine. Fifteen grains (1 Gm.) of quinine hydrochloride will dissolve in 30 minims (2 c.c.) of water if 6 to  $7\frac{1}{2}$  grains (0.4 to 0.5 Gm.) of antipyrin be added. Laveran is authority for the statement that hypodermic injections thus given are less painful than where the bihydrochloride is used.

Quinine and urea hydrochloride is used in a sterile 50 per cent. solution.

Solis-Cohen, administering this salt in cases of pneumonia, inserts the needle through skin previously painted with tincture of iodine, deeply into a muscle, and takes great care to empty the syringe thoroughly, in order that none of the solution shall drop on the skin when the needle is withdrawn. The point of puncture is then sealed with iodoform collodion. He thus injects as much as 25 grains (1.6 Gm.) of the salt (containing 59 per cent. of alkaloidal quinine), without any ill result.

When the bisulphate of quinine is employed, 1 grain (0.06 Gm.) of tartaric acid should be added for each 5 grains (0.3 Gm.) of the salt, in order to prevent precipitation of the latter by the alkaline juices of the tissues before its absorption can occur. Lente's solution of the bisulphate is as follows: Quinine bisulphate, 50 grains (3.3 Gm.); diluted sulphuric acid, 100 minims (6.6 Gm.); water, 1 ounce (30 Gm.); dissolve with heat, filter, and add 5 minims (0.3 Gm.) of phenol.

Grimaux and Laborde recommend a solution of the hydrochlorosulphate of quinine, made by adding 75 grains (5 Gm.) of this salt to 90 minims (6 Gm.) of sterilized distilled water. Very little pain is caused by this preparation.

Where no quinine salt other than the sulphate is available, this compound should be placed in 6 times its weight of water and dilute sulphuric acid gradually added until solution has been effected. Another formula which has been suggested is: Quinine sulphate, 1 dram (4 Gm.); morphine sulphate,  $\frac{1}{2}$  grain (0.03 Gm.); diluted sulphuric acid, 40 minims (2.6 Gm.); distilled water, 1 ounce (30 Gm.); mix and filter. Each dram (4 Gm.) of this preparation contains  $7\frac{1}{2}$  grains (0.5 Gm.) of quinine.

**Intravenous.**—In pernicious forms of malaria, the intravenous route gives the best therapeutic results. Not only does the drug act immediately and in maximal concentration on the parasites, but local discomfort is almost invariably entirely obviated. All necessary antiseptic and aseptic precautions having been taken, and the usual constricting band applied, the needle may be placed directly in the vessel selected without previous skin incision. Baccelli uses the following solution for intravenous administration:—

*R. Quininae hydrochloridi* ..... gr. xv (1 Gm.).  
*Sodii chloridi* . gr.  $\frac{5}{4}$  (0.075 Gm.).  
*Aqua destillata*,  
 q. s. ad ..... f3iiss (10 Gm.).—M.

The solution should be boiled and filtered before use, and should be given while warm, and injected very slowly, as quinine in concentrated form acts powerfully as a cardiac depressant. The amount of quinine to be injected may vary from 6 to 15 grains (0.4 to 1 Gm.). If 15 grains be given, a solution of the drug of approximately 1:5000 strength will be formed in the blood-stream.

An isotonic solution of the basic hydrochloride of quinine for intravenous injections should contain about 75 Gm. (2½ ounces) of the salt to the liter (quart). In a solution containing less than this percentage 1.25 Gm. (19 grains) of sodium chloride must be added in place of each lacking gram (15 grains) of the quinine salt, in order to make the solution isotonic. Chappelle (*Semaine médicale*, Aug. 19, 1908).

The dihydrochloride, urea, and hydrochlor-sulphate of quinine and the dihydrochloride and acid hydrobromide of cinchonine are highly soluble and have no immediate effect on blood serum in the strongest concentrations. The acid hydrobromide

and bisulphate of quinine cause very slight precipitation in serum in 1:10 solution and none in 1:100. The remaining salts produced turbidity even in dilute solutions. None of the salts caused any increased tendency of the blood to clot and all of the more soluble ones were found to be relatively effective in destroying water paramecia, quinine acid hydrobromide and the dihydrochloride being the most active. Experiments on animals showed the soluble salts to be relatively non-toxic by intravenous injection. The dihydrochloride and the acid hydrobromide were also given to man in a few cases of malignant malaria and of the latter a safe dose was found to be from 0.6 to 1 gram in 10 per cent. solution, while half as much of the former usually produced marked cinchonism. In two cases the intravenous injection of quinine prevented death from coma. L. Rogers (*Brit. Med. Jour.*, Sept. 22, 1917).

**INCOMPATIBLES.**—Quinine salts are precipitated by the addition of tannic acid, which leads to the formation of the practically insoluble quinine tannate; by alkalies, ammonia, and lime water, which neutralize the acid in combination with the quinine, and thereby set free the practically insoluble uncombined alkaloid, and by preparations containing iodine, such as potassium iodide and Donovan's solution.

**CONTRAINDICATIONS.**—In inflammatory conditions of the middle or internal ear as well as of the meninges and brain-tissue (cerebritis) quinine is likely to do harm through the congesting effect it is believed to produce in these areas. Permanent impairment of the hearing may result from the administration of quinine in aural inflammations. In epilepsy quinine is likely to aggravate the condition.

In the presence of gastritis or abnormal gastric irritability the use of

quinine by the mouth is contraindicated. The drug need not, however, be abandoned, but should be given by rectum or, if practicable, preferably by intramuscular injection.

In a few individuals there is encountered idiosyncrasy of such degree as to prohibit the use of the quinine. In addition to severe tinnitus and headache, there may be present a tendency to general prostration, difficulty of respiration, or actual collapse. Nervous disturbances and skin eruptions may be obviated to a certain extent by simultaneous use of bromides, ergot, and arsenic.

In infantile eczema quinine is considered prejudicial, and in nephritis a possible harmful effect is to be thought of. Beard states that in the elderly, and especially in patients with urethritis, specific or otherwise, irritability of the bladder, followed by retention of urine, may be caused by quinine.

Pregnancy does not formally contraindicate quinine; the drug should, however, be used with caution.

That miscarriages are common in women suffering from malaria cannot be denied, nor can it be denied that, in rare instances, the quinine itself acts as an abortifacient, but only in those cases possessing an idiosyncrasy. In twenty years the author has never been deterred from the exhibition of quinine by reason of pregnancy and not seen a case of miscarriage due to the ingestion of the drug. *Per contra* he has seen miscarriages occur a number of times in cases where quinine was not given for fear of its results. The uterus tends to expel its contents in all fevers; therefore, whatever speedily eliminates the fever or its toxins is physiologically indicated in the pregnant state as well as in any other. T. S. Dabney (N. O. Med. and Surg. Jour., Oct., 1903).

The author has treated 50 to 60 pregnant women suffering from malaria with 3-grain (0.2 Gm.) doses of quinine to begin with, three or four times a day, increased to 5 grains (0.3 Gm.) whenever necessary, without untoward result. He combined with each dose 5 minims (0.3 c.c.) of tincture of opium. A. M. Mudaliar (The Antiseptic, Oct., 1909).

### PHYSIOLOGICAL ACTION.—

The action of quinine practically represents that of cinchona, as well as that of the other alkaloids contained in the crude drug. Since quinine is the preparation of cinchona most frequently used, it will be taken as the standard in the description of the physiological effects, reference being made to cinchona or the other alkaloids only where their action diverges from that of quinine.

**Locally**, quinine salts act as irritants when applied in concentrated solution to mucous membranes or open surfaces. Subcutaneous injections are notoriously irritating. Upon the intact skin, however, but little effect is produced except, in some instances, slight roughening. Dilute solutions of quinine and urea hydrochloride, injected subcutaneously, or stronger solutions applied to mucous membranes, have been found not only to be practically devoid of irritating properties, but to induce a marked degree of local anesthesia, which may persist for a number of hours.

Quinine can be classed as a general protoplasmic poison, since if present in appropriate concentration it is capable of arresting the functional activity of every form of living cell, animal or vegetable, and shows no particular affinity for any special type of protoplasm, as is, on the contrary, the case with many other alkaloidal poisons. Small

amounts generally cause an initial increase in protoplasmic activity, which is soon followed by depression and ultimately by paralysis. Larger amounts, on the other hand, may cause immediate death. The variety of cell paralyzed by quinine in smallest amount is the unicellular animal organism or protozoön, and of the protozoa, in turn, the plasmodium of malaria is the most susceptible to the toxic action of the drug. Bacteria are also inhibited by quinine, although not as easily as the protozoa. Molds, on the other hand, are not acted upon by the drug. Leucocytes are influenced in much the same way as the protozoa, a fact first emphasized by Binz. Not only do leucocytes, when brought into contact with small amounts of quinine, cease their ameboid movements and lose their property of diapedesis through the capillary walls, but their protoplasm becomes filled with dark granules, and ultimately they are disintegrated in considerable numbers. While it is not considered probable that therapeutic doses of quinine, as administered in man, arrest the activity of phagocytes, an appreciable reduction in the number of leucocytes in the blood has been observed to take place.

The activity of certain unorganized ferments, including the oxidizing ferment in blood, has been shown to be hindered or abolished by quinine.

#### **General Effects. Nervous System.**

—Moderate doses of quinine exert no obvious influence upon the nervous system. The effects of massive doses have been ascertained chiefly through animal experimentation, and consist, essentially, of preliminary stimulation, followed by depression. Excessive doses in man, however, are frequently observed to induce a sensation of fullness in the head, which has been inter-

preted as denoting a dilatation of the cerebral vessels.

The spinal cord in the frog shows a brief period of abnormal excitability under quinine; this is promptly followed by depression and paralysis. Similar effects are believed to occur in the cord of mammals after large doses of the drug.

The peripheral nerves, motor and sensory, are totally uninfluenced by quinine, when taken internally. The local anesthetic effect of the hydrochloride of quinine and urea has not as yet been satisfactorily explained.

*Circulation.*—Quinine in moderate doses tends to increase slightly the cardiac rate and raise the blood-pressure,—an effect believed due mainly to direct stimulation of the heart-muscle and the walls of the arterioles. With large doses—amounts exceeding 1 dram (4 Gm.) in the adult human subject—the stimulation is soon replaced by distinct depression. The cardiac rate is lowered, the individual beats are weakened, and the blood-pressure shows a pronounced fall. In children, an intermittent pulse may be caused by full doses of quinine.

Action of various quinine salts on the isolated heart of the tortoise investigated. The salts used were: the hydrochloride, citrate, valerate (valerianate), hydrobromide, and neutral sulphate. Small amounts of quinine were found favorable to the heart action, whereas large amounts were distinctly unfavorable. An increase of tolerance to quinine was sometimes noticed, the heart easily supporting the action of a strong dose after the application of a weak one. In general, all the salts caused slowing of the beats. The statement hitherto accepted that any accelerating effect of quinine on the heart is due to an action on the extrinsic nervous cardiac mechanism is thereby

confirmed. All the salts diminished the amplitude of the beats when applied in large amount. In small amounts the hydrochloride was found to increase the amplitude, the hydrobromide first to increase then diminish it, and the other 3 salts to diminish it from the beginning. At a certain level of toxicity the phenomenon of "reversed quinine action" sometimes appeared, especially with the sulphate: A solution at first toxic became innocuous; then stimulated the heart. The results of the experiments argue neither in favor of an exclusive action of the drug on the intracardiac ganglia nor on one exclusively on the heart muscle; it is difficult to conceive of a paralyzing effect exclusively on the myocardium, since, without change in the rate, a considerable increase in the systolic force was often noticed. The results also support the opinion of Schmiedeburg, Meyer and Gottlieb, Poulsson, and v. Tappeiner, that the hydrochloride of quinine should be used in preference to the sulphate in clinical medicine. De Arric (Ann. et Bull. de la Soc. des Sci. méd. et nat. de Bruxelles, vol. lxx, No. 6, 1912).

*Blood.*—The effects of quinine on the leucocytes and oxidizing ferment of the blood have already been referred to. The quantity necessary to arrest the movements of leucocytes examined on a warmed slide is 0.5 to 1 in 1000; but according to Binz, as little as 1 to 20,000 is sufficient to reduce the number of white corpuscles in the circulating blood and to arrest diapedesis. The restraining influence of quinine on inflammatory processes has been attributed to this action on the leucocytes. It has also been shown by Wilson and others that small doses of quinine favor phagocytosis, while doses exceeding 10 grains (0.6 Gm.), on the contrary, interfere with it. According to some, the number of red corpuscles in the blood is increased by continued admin-

istration of quinine. Toxic doses are said to alter the coagulability of the blood. Drawn blood to which quinine is added loses the property of decolorizing indigo and will no longer give a positive guaiac test.

When the minimum fatal dose of quinine is given to rabbits the leucocytes assume the rounded form which is characteristic of the early stage of the quinine action in drawn blood. E. Maurel (Arch. de méd. expér. et d'anat. pathol., vol. xv, 1903).

If large doses of quinine are administered, phagocytosis is inhibited, but if smaller doses are given it is very markedly increased, the increase amounting to as much as 25 per cent. over the normal. The quantity of quinine producing this increase is equivalent to about  $\frac{1}{2}$  grain (0.032 Gm.) circulating in the blood of a man weighing 170 pounds, i.e., that quantity of quinine which would probably be taken into the circulation from a dose of from 2 to 3 grains (0.013 to 0.2 Gm.) of the sulphate. T. M. Wilson (Jour. of Physiology, Sept. 2, 1907).

Research on blood of dogs given quinine for from two to four months. Neither the color, transparency, toxicity, freezing point, proportion of chlorides, sulphates, nitrogen, ash, etc., of the blood-serum showed any modification. The only change detected was a slight increase in the specific gravity and in the quantity of organic elements. D. de Sandro (Riforma Medica, April 4, 1910).

*Respiration.*—The effects on the breathing are similar to those on the circulation. Poisonous doses given subcutaneously to animals usually kill by paralyzing the respiratory centers; the heart action is weakened at the time of death, but its beats may persist for an appreciable interval after the respiration has ceased. Toxic doses given intravenously, however, may produce death through direct cardiac paralysis.

*Alimentary Tract.*—The extremely bitter taste of quinine—noticeable even in a 1:10,000 dilution—brings it into the category of “bitter tonics.” When taken by the mouth, quinine or cinchona preparations improve the appetite, increase the flow of saliva and gastrointestinal secretions, and tend to excite peristalsis. Excessive amounts, however, or repeated smaller doses, prove irritating and give rise to symptoms such as nausea, eructations, vomiting, colicky pains, and diarrhea.

Cinchona preparations, owing to the cinchotannic acid they contain, tend to exert an astringent action and may produce constipation.

*Muscles.*—Quinine in small amounts is capable of increasing the power of muscular contractions; exhaustion upon continued activity, however, occurs sooner than under normal conditions. Large amounts weaken the muscular function and place the muscle-tissue in a condition of rigor similar to that induced by caffeine. The action of quinine on the *uterus* has been utilized in therapeutics. In pregnancy the drug tends to excite the contractions of this muscle, and it has even been asserted to produce abortion, though definite facts in this direction appear to be lacking. In labor the uterine contractions are sometimes strengthened by quinine, and the tonicity of the organ is believed to be increased. The action of quinine on the uterus appears to be exerted directly, *i.e.*, without the intervention of nervous influences, although some authors deny this, and consider the matter as yet entirely unsettled.

*Kidneys.*—The quantity of urine excreted is in some instances slightly increased.

Experimental and chemical research which showed that quinine in

small doses, continued for some time, does not injure the kidneys seriously, but that after several months these organs seem to yield more readily to external influences, responding more rapidly with albuminuria, etc., to factors which would not affect the sound kidney. Microscopic examination of the organs after several months revealed, further, certain lesions in the secreting portion of the kidneys. Long-continued, small doses of quinine may be regarded as harmless unless administered longer than several months. Ferrannini (*Riforma Medica*, March 21, 1910).

A dose of 15 grains (1 Gm.) of quinine hydrochloride causes an early increase in the amount of water excreted in the urine. This is followed within twenty-four hours by a marked decrease, accompanied by an increase in the excreted pigments, largely urobilin. There is then an approximate return to the normal elimination of water and pigment, the phase being almost completed in one week. Graham (*Annals of Trop. Med. and Parasit.*, Dec. 30, 1911).

*Organs of Special Sense.*—Even moderate amounts of quinine may produce a disturbance of the auditory apparatus manifested as roaring or ringing in the ears, not infrequently with a slight degree of deafness. With larger amounts dizziness and unsteady gait, due to vestibular involvement, and diminished visual power, due to an effect on the retinae, may accompany the disturbance of hearing, which may itself proceed to complete deafness. In the milder cases of ophthalmic involvement disturbances of color vision and contraction of the visual field are the chief features, but in other instances complete amaurosis, lasting some days or weeks, has been known to supervene. Pronounced narrowing of the lumen of the retinal vessels, with pallor of the optic disk, accompanies these disturb-

ances. In some cases degeneration of the retinal ganglion-cells has been found to result, and optic atrophy is also known to have occurred. The precise cause of these special sense disturbances is still somewhat in doubt. It has been the habit to regard them as due primarily to extreme changes in vascular caliber, with or without the accompaniment of hemorrhage, as, *e.g.*, in the middle and internal ear, but recent researches appear to have shown that the effects are due throughout to a direct action on the nervous structures concerned, the vascular changes being merely an additional disturbance devoid of special significance. In the ear the tendency seems to be toward congestion, which may attain such a degree as to lead to permanent impairment of hearing through inflammation of the drum membrane, whereas in the eye marked vasoconstriction is the rule.

*Temperature.*—Upon the normal body temperature, quinine exerts little or no effect. In the presence of fever, however, a distinct antipyretic effect is exerted, though this is not, in general, as pronounced as that occasioned by the coal-tar drugs. Its cause has been shown by Gottlieb not to reside in an action on the nerve-centers of heat regulation, and is now believed to be a depressing action of the drug on metabolism in general, with consequent diminished production of heat. The fact that the normal temperature is practically uninfluenced by the drug necessitates, in justification of this view, the assumption that metabolism is more easily affected by the drug in fever than normally, and the suggestion has been made, as stated by Cushny, that it is to the action of the "fever poisons" themselves on the tissues that this increased susceptibility to the action of quinine is

due. That quinine lowers temperature by inhibiting bacterial pullulation can hardly be given more than partial credit, as its antiseptic action does not appear to be sufficiently powerful for this purpose. In malaria, however, destruction of the organic cause of the pyrexia is undoubtedly the chief factor in the antipyresis induced.

*Metabolism.*—Diminished destruction of the body proteids is a characteristic effect of the ingestion of quinine, even in small amounts. Although for the first few hours after the initial dose there may occur an increased elimination of nitrogenous products in the urine, this is soon followed by a pronounced decrease, which bears particularly upon the urea and uric acid content, and may attain 39 per cent. of the total nitrogen elimination. The drug thus appears to lead to an economy of the proteins. Since the oxygen intake and carbon-dioxide output, however, remain unaltered, it seems evident that other forms of metabolism, such as are concerned in muscular activity and the production of heat, and therefore involve the consumption of carbohydrates and fats, are not affected by quinine.

The quantity of sulphur and nitrogen eliminated in the bile in twelve hours, as well as the quantity of bile secreted and its dried residue, is not appreciably altered by the action of quinine, even in large doses. A. Benedicenti (Arch. Ital. de Biol., March 28, 1903).

Quinine hydrochloride administered to rabbits and guinea-pigs in dosage proportional to that used for man in the prophylaxis of malaria. The growth of the quinized animals was distinctly impaired as compared with control animals receiving only injections of physiological salt solution. Prolonged use of quinine is not an

innocuous procedure, as it may prevent the growth of young animals, and subsequently lower their power of producing immune bodies and resisting microbic infection. Graziani (*Archiv für Hygiene*, cited in *Med. Times*, Feb., 1912).

**Absorption and Elimination.**—Quinine is rather rapidly absorbed from the alimentary tract, as is shown by the fact that, upon ingestion of its most soluble salts, it may be detected in the urine within fifteen minutes. In the blood the maximal amount of quinine is present between three and six hours after ingestion. A considerable portion of it is destroyed in the system, as it has been found that only one-third of the dose taken is eliminated in the urine. In man it appears in the last-named excretion unchanged and may continue to be present in it for as long a period as seventy-two hours (Cushny), although one-half the total amount may be eliminated in the first six hours.

All but about 12 to 14 per cent. of quinine ingested is destroyed in the organism of the dog. This destruction is not less at the beginning of a four-week investigation than it is at the end. The undestroyed portion appears in the urine in the form of a basic metabolic product of quinine. Merkel (*Archiv f. exper. Pathol. u. Pharmak.*, Bd. xlvii, Heft 3 u. 4, 1902).

The therapeutic action of quinine depends rather upon the amount of the drug in the circulation than upon the quantity assimilated by the tissues. Its maximum effect, therefore, occurs about six to nine hours after ingestion in the afebrile individual and from nine to twelve hours after in fever patients. Arnaud (*Marseille méd.*, No. 11, p. 356, 1905).

The absorption of quinine is completed, when it is taken on an empty stomach, in twelve hours, but when it is taken on a full stomach the

absorption is completed only within twenty-four hours. The blood quickly yields the drug to various organs. Small quantities of quinine are stored up in the liver, bile, kidney, and brain, and to a less extent in the spleen; but in the lungs, cervical glands, and muscles, quinine cannot be demonstrated.

Quinine is excreted as such in an unchanged condition in the urine, with probably only a small amount of its transformation products. Kerner and Merkel found several such products—the so-called amorphous quinine—but the authors did not succeed in finding them. It is very probable that these bodies, when found, were formed by the action of strong chemical reagents used in the attempt to separate them. The quinine absorbed disappears relatively rather quickly from the organs. In the second twenty-four hours, the quantity remaining is very small, and after seventy-two hours the excretion is completed or only a trace is discoverable. The larger proportion of absorbed quinine (about  $\frac{2}{3}$  to  $\frac{3}{4}$ ) is decomposed, the remainder ( $\frac{1}{4}$  to  $\frac{1}{3}$ ) excreted. The excretion is confined to the urine; in the feces there is very little excreted; in the sweat, none.

In normal individuals, during prolonged quinine treatment, the excretion presents extraordinary variations on different days, even when examination of the feces shows that the absorption on these days was equal. Giemsa and Schaumann; translated by Chatterjee (*Calcutta Med. Jour.*, April, 1909).

Quinine is taken up by the blood within ten or fifteen minutes after hypodermic injection; the greater part of it reaches the kidneys and the liver, while in the other internal organs the tests for quinine remain negative. The spleen is reached later, after an interval of about fifty minutes; most of the quinine injected is then found in that organ, where it remains longer than in any other part of the body. Quinine can be



demonstrated in the spleen even twenty hours after the injection. The drug is more active in malaria when injected hypodermically than when taken by mouth. It is probable that the lesions which occur in the spleen in malaria still further favor the retention of quinine in that organ and therefore increase the duration of the action of the drug between attacks. De Sandro (*Riforma Medica*, Nov. 8, 1909).

**Action of the Other Alkaloids of Cinchona.**—Of these only cinchonine, cinchonidine, and quinidine need be considered. Cinchonine and cinchonidine differ from quinine in causing greater stimulation of the central nervous system, which, if the dose be sufficient, may be excited to epileptiform convulsions. Cinchonidine is considered more convulsive than cinchonine. In other directions the effect of these two alkaloids is practically that of quinine, but quantitatively less marked; the antipyretic power of cinchonine and cinchonidine is said to correspond to  $\frac{4}{10}$  and  $\frac{1}{10}$ , respectively, of that of quinine.

Quinidine is not convulsive and exerts practically the same effects as quinine, though it is slightly weaker.

**UNTOWARD EFFECTS AND POISONING.**—The unpleasant phenomena frequently resulting from the use of full doses of quinine—exceeding 10 grains (0.6 Gm.)—have already been in part mentioned. The commonest of these are a sensation of fullness in the head, which may amount to actual headache; a roaring sound in the ears, and slight impairment of hearing. Other effects include skin eruptions, vertigo, temporary blindness or complete deafness, epistaxis, discomfort in the region of the stomach, vomiting, diarrhea, delirium, and vesical irrita-

bility. Any of these disturbances may be occasioned even by small doses in individuals with an idiosyncrasy to the drug.

Quinine may produce tinnitus aurium, deafness, and headache. Vertigo, vomiting, vesical irritation, uterine contractions, and eruptions occasionally result from its use. General weakness, collapse, complete deafness, and blindness have been some of the severe accidents following the administration of quinine. These symptoms are as a rule overcome by stimulants and diuretics. A. Martinet (*Presse méd.*, April 19, 1902).

Case of a woman aged 28 years suffering from a severe attack of estivoautumnal malarial fever. In spite of a history of previous untoward results from quinine sulphate, a 5-grain (0.3 Gm.) capsule of it was administered. After half an hour the pulse became a little irregular, the face grew pale, and she commenced to complain of slight dyspnea. These symptoms rapidly grew worse, the pulse became imperceptible at the wrist, and the breathing very slow and labored. The abdomen became shrunken, the eyes looked lusterless, and the pupils did not respond to light. Hypodermics of brandy, strychnine, and nitroglycerin were promptly administered. Electricity was given intermittently and artificial respiration practised from time to time. The patient remained profoundly unconscious for fully eight hours. No rash occurred. The entire brunt of the drug seemed to have fallen on the pneumogastric nerve or else on the sympathetic system. Two years later, the patient developing another sharp attack of malaria, the hydrochloride of quinine was given in 5-grain (0.3 Gm.) doses every three hours. No unhappy sequelæ resulted, the only effect noticed being a heightened arterial tension. The hydrochloride was thereafter taken on a number of occasions with impunity. T. S. Dabney (*N. O. Med. and Surg. Jour.*, Oct., 1903).

Case reported of a patient who had been treated some years before with quinine for malaria. On examination, the spleen was found enlarged and somewhat painful. Quinine sulphate, 9 grains (0.58 Gm.), was ordered to be taken once daily. A few hours later the temperature had risen 4.2° F. After giving further doses, it was concluded that the fever was due to the quinine. As soon as the patient was put on a mixture of ergotin and piper nigrum, her fever failed to appear, and she made an uninterrupted recovery. The writer concludes that the fever is due to some chemical changes in the blood acting on the heat-dissipating apparatus in persons who have had malaria. A. L. Goodman (Med. Record, Dec. 1, 1906).

Case of a woman of 30 to whom intramuscular injections of quinine had been given fifteen years before for puerperal fever, with no unpleasant results except the formation of small nodular cysts and an occasional abscess at the sites of injection. Recently, a cachet containing 0.1 Gm. (1½ grains) of quinine sulphate was taken on account of a light attack of grippe, with slight fever. Soon after, there developed tinnitus, nausea, bilious vomiting, and a macular eruption accompanied with itching. The symptoms subsided rather promptly, but reappeared on three subsequent occasions after the same dose of the drug. The lately noticed intolerance might be considered an anaphylactic phenomenon. A. P. Cabra (Rev. de Med y Cirur. Pract., May 7, 1912).

According to Clemesha, incomplete ocular cinchonism is not rare; some paresis of accommodation is observable in a considerable percentage of cases in an hour after 20 grains of quinine have been taken. Photophobia may also be present. Blindness, when it occurs, may appear suddenly, and is associated with marked contraction of the vessels supplying the retina and optic nerve,

together with serous exudation, as shown by Holden in dogs. Where this condition continues for a sufficient length of time, degeneration of the retinal ganglion cells, atrophy of the optic nerves and tracts, and permanent obliteration of the lumen of the vessels may take place. Such a result is, however, very rarely observed in human subjects.

Case of a woman with puerperal septicemia who took during eight days 150 to 180 grains (10 to 12 Gm.) of quinine. Visual hallucinations then occurred as a feature of her delirium, and in a few hours she became quite blind. The pupils were widely dilated, and reacted feebly to light; the disk was pale, with a sharp border; the retinal arteries were extremely constricted and most of them bloodless, while in the macular region was a rounded, pale-red spot about one-third the size of the optic disk. After a fortnight the eyes began to improve, nystagmus appeared, and the patient could count fingers; the blood in the arteries was again visible. The visual fields are still much constricted concentrically; the patient can distinguish blue, but is blind for red and green. The treatment consisted of nux vomica with nitroglycerin, and occasional amyl nitrite inhalations, besides, of course, stopping the quinine. The total number of recorded cases is under 100, of which about one-half became quite well. The onset in all cases is sudden, and associated with tinnitus aurium and deafness. This susceptibility may be constant or merely temporary, due to lowered vitality at the time. The primary lesion is in the ganglion-cell layer of the retina; the circulatory disturbance plays a subsidiary rôle in the causation of the blindness by depriving the already damaged cell of its nutritive supply. The extreme retinal vascular constriction may be a reflex, serving to preserve the delicate nervous elements by cutting off the blood

charged with quinine. G. H. Mathewson. (*Montreal Med. Jour.; Medical Chronicle*, April, 1905).

Case of a woman 36 years old who took 6 Gm. (92 grains) of quinine within three days and then suddenly became deaf and blind. Hearing returned within twenty-four hours, but the first trace of light perception returned ten days later, and it was about two months before her vision completely returned. The fundus exhibited a picture similar to that seen in embolism of the central artery of the retina followed by that of atrophy of the optic nerve. The visual field, when it could first be taken, was concentrically contracted, then gradually enlarged, until in the course of two months it was normal for white. A marked and permanent injury of color perception remained. Seeligsohn (*Berl. klin. Woch.*, March 4, 1907).

Skin eruptions due to quinine may be of various types. They are most commonly erythematous, scarlatiniform, or urticarial, but may also be petechial, erysipelatous, vesicular, papular, or gangrenous. Itching is not infrequently an annoying accompaniment. Where the entire surface is affected, some degree of fever may be present. Wood observed desquamation as a sequel in 14 out of 61 cases, and involvement of mucous membranes in 11 out of the 14. He emphasizes the fact that the dosage, age, and sex have little influence on the incidence of eruptions, the chief predisposing factor being idiosyncrasy. Bock reported the case of a man who, upon taking 5 1-grain (0.06 Gm.) pills of quinine at hourly intervals, not only developed an erysipelatous facial eruption, but showed signs of collapse and subsequently went into delirium; while Stelwagon refers to a case in which 3 pills, each containing  $\frac{1}{16}$  grain (0.004 Gm.) of the alkaloid, brought on a

scarlatinoid eruption, followed by desquamation. Rizü and Floyer have seen urticarial eruptions accompanied with dyspnea induced by small amounts of quinine.

Case of a man aged 53 years who was ordered 2 grains (0.13 Gm.) of quinine with  $\frac{1}{60}$  grain (0.001 Gm.) of arsenic three times daily as a tonic during convalescence. Twelve hours after the first pill an intense erythema appeared all over the body, with itching and puffiness of the face. Abundant desquamation followed, very similar to that of scarlet fever, and continuing for weeks. H. A. Hare (*Therap. Gaz.*, May, 1901).

Case of eruptive phenomena due to the ingestion of minute quantities of quinine. Patient had had 20 to 25 attacks of scarlatiniform erythema, followed by branny, lamellar, and sheet-like desquamation, with more or less itching, and running a course of several weeks. The cause of the first three or four outbreaks was not suspected. The patient, not feeling well, consulted a physician, who prescribed quinine in the average dose. This was immediately followed by a scarlatinous rash, which was thought to represent a second attack of scarlet fever. When the exfoliation was practically ended, as he was not feeling well, a tonic containing quinine was given, the result being another attack. Some time later, desiring a tonic, he consulted another physician and told him of his extreme susceptibility. The physician considered it nonsense and prescribed a mixture, the vehicle of which was the elixir of calisaya. Each dose contained  $\frac{1}{4}$  grain (0.008 Gm.). One dose resulted in an outbreak. Further attacks resulted from the tasting of some bitter wine of iron being prepared in a drug-store, from a new summer drink proffered by friends, from a cocktail flavored with bark, from a single dose of compound syrup of hypophosphites, from a rhinitis tablet, from a toothwash containing an infinitesimally small quan-

tity of calisaya, from a quinine hair tonic, etc. Henry Stelwagon (Jour. of Cutaneous and Genito-Urin. Dis., Jan., 1902).

Case of almost fatal poisoning by 6 grains (0.39 Gm.) of quinine. A healthy man 27 years old was brought to a hospital in a condition of collapse. Less than an hour before, he had applied to an apothecary for medicine for a "cold," and had been given 5 pills said to contain quinine. He had taken 2 pills at once, and about fifteen minutes later had noticed a burning of the skin and palpitation. To these symptoms were soon added vertigo, faintness, tachycardia, and great weakness. When admitted he complained of some abdominal pain and of intense weakness. His face was pale and covered with cold sweat, his respirations shallow, and no pulse could be felt, though on listening over the precordium faint heart-beats, too rapid to be counted, could be heard. Upon vigorous stimulation, together with external heat, half an hour later the radial pulse could be felt, although still very feeble, and the count at this time showed 180 beats to the minute. The burning and itching of the skin, which had been noticed early, gradually increased, and, about an hour after admission, there appeared over trunk, extremities, and face a diffuse scarlatiniform rash, with much swelling of the skin, especially about the face. The temperature was 100° F. (37.8° C.). On the following morning the eruption had nearly disappeared. Two days later the pulse was normal in rate and of fair force, but was somewhat irregular. The patient still felt very weak. There was still some itching of the skin. At no time during the attack was there either ringing of the ears or deafness. The remaining 3 pills proved, on analysis, to contain each 3 grains (0.2 Gm.) of quinine sulphate. The patient stated that there existed in his family a distinct idiosyncrasy toward quinine. L. A. Conner (Med. Record, April 4, 1903).

A man of 35 took what he believed to be a laxative pill one evening after dinner. Within twenty minutes he felt a tingling sensation, which he knew by experience to be the result of quinine. This was rapidly followed by the appearance of large wheals in different parts of the body, which quickly coalesced and gradually became purplish. It became necessary to give morphine owing to swelling and pain. The next day bullæ were forming, the pulse was 112, and the temperature 101.5° F. (38.4° C.). In a few days the patient was well. Some of the bullæ had been as large as the palm of the hand. M. Goltmara (Med. Record, Aug. 22, 1903).

Case of a man aged 35 years who, about one hour after taking 2½ grains (0.16 Gm.) of quinine bisulphate, complained of a "sinking" feeling in the abdomen. Flushing of the face, intense irritation, and discomfort then began and gradually spread throughout the body. This was quickly followed by a rapidly spreading erythematous rash, most marked on exposed portions of the body. The skin everywhere was hot, hyperemic, and dry; the temperature, however, was subnormal. There were distracting tinnitus and frontal headache, but no amaurosis. The heart's action was seriously weakened; there were palpitation and shortness of breath. Later he had a syncopal attack while trying to rise from his bed. After nine hours all the symptoms had cleared up with the exception of headache. A. C. Parsons (Lancet, Nov. 14, 1908).

Case of a woman known to be very susceptible to quinine who took 2-dram (8 Gm.) doses of a preparation known to contain but ¼ grain (0.016 Gm.) to the dram (4 Gm.). A rash appeared, and spread over the entire body. She was advised to continue with the preparation in the hope that she might become accustomed to it. During the next two days the condition remained the same; it was worse at night. The drug was then stopped.

On the fourth day the hands, legs, and ankles were greatly swollen, the palms red and shining, while the fingers and toes were stiff, numb, and distinctly cold to the touch. By the seventh day desquamation began, the epidermis separating in large strips and flakes, with almost casts from the toes. During the fourth week, this was completed. W. Gripper (*Brit. Med. Jour.*, July 3, 1909).

Case of a woman who was given a 5-grain (0.32 Gm.) capsule of quinine. In ten minutes her face began to swell and an eruption appeared on the entire body, with intense itching. Her teeth were chattering and she said she felt cold. The swelling of the face continued until the eyes were almost closed, and the eruption resembled a crop of flea-bites. R. E. Davis (*Amer. Jour. Clin. Med.*, April, 1912).

In doses of 30 to 60 grains (2 to 4 Gm.) quinine may, in addition to deafness and staggering gait, produce well-marked delirium, resembling that caused by alcohol. The patient is talkative and restless, with the face red, skin hot, and pulse accelerated (Briquet). In other instances, such doses may bring on a state of quiet dreaminess or actual stupor, with general prostration. According to Gubler, quinine delirium is the result of cerebral ischemia.

Case of a man in whom even small doses of quinine produced chills, a considerable elevation of temperature, delirium, dryness in the throat, thirst, vomiting, and a severe dermatitis accompanied by a scarlatiniform eruption. Gorbatsheff (*Med. Obosrenie*, March, 1901).

Albuminuria, hemoglobinuria, and hematuria occasionally occur as a result of quinine administration,—the latter especially in malarial cases.

Case of a woman who had been treated several months before with large doses of quinine, which she had borne well. Upon recurrence of

the disease, she was given the remedy again. Immediately after the first dose of 0.3 Gm. (4½ grains) she complained of bad vision, ringing in the ears, and vomiting. On the following day she was directed to take only half a dose once a day. Next morning her entire face was swollen and so edematous that the eyes could scarcely be seen. The margins of the lupus erythematosus from which she suffered were covered with thick blood-crusts, while the lesions were permeated with numerous little hemorrhages. There was also extensive purpura hæmorrhagica in parts free from the disease, and a severe hemorrhage from the conjunctiva of the right eye. She suffered from dyspnea, hematemesis, bloody diarrhea, hematuria, and bleeding from the mucous membranes of the mouth and nose. Recovery took place after a few days. Salomon (*Münch. med. Woch.*, Aug. 25, 1908).

Gastric pain and vomiting may be produced even by very moderate doses of quinine. In general, however, doses of 15 grains (1 Gm.) and upward are required to produce these effects. In the intestinal canal, either diarrhea or constipation may result from the use of quinine.

Acute poisoning by quinine sufficiently pronounced to endanger life is a rare occurrence. Manquat refers to cases in which 8, 9, 12, 30, and even 41 Gm. (120, 135, 180, 450, and 615 grains) were taken within a few days without a fatal result. On the other hand, Baills reports that, of 2 patients who had each ingested 12 Gm. (180 grains) of a 5 per cent. solution of quinine, 1 died, while the other recovered. In a case recorded by Récamier, 5 Gm. (75 grains) taken in a period of twelve hours caused death. Where massive doses are ingested the percentage of the drug actually absorbed into the system is always a

matter of doubt, especially since the salt of quinine generally used, the neutral or basic sulphate, is but slightly soluble, and is scarcely absorbed at all from the intestine, with its alkaline juices. The average fatal dose of quinine is frequently stated as 120 grains (8 Gm.); but this should not be construed as applying to subcutaneous injections. That the danger of massive injections of quinine cannot be wholly disregarded was illustrated in a personal experiment in which a subcutaneous injection of 1 grain (0.06 Gm.) of quinine bisulphate in a small guinea-pig produced, after preliminary excitement, oscillatory movements (especially of the head), progressive motor paralysis, and death from respiratory failure in twenty minutes.

In cases of fatal poisoning in human beings the symptoms noted have been chiefly auditory and visual disturbances, nausea and vomiting, mental confusion, delirium alternating with unconsciousness, occasionally convulsions, collapse, coma, and death, the latter usually by arrest of respiration.

A patient swallowed, evidently with suicidal intent, about 240 grains (8 ounces) of quinine sulphate in solution. Within two minutes retching and vomiting began, which were favored by the prompt administration of an emetic. This was soon followed by almost total unconsciousness, slow and labored respiration, and a barely perceptible pulse, which, under very active stimulation, would return for a time only. A few hours later convulsions affecting mainly the lower extremities came on, and this was soon followed by death. Post-mortem examination showed the blood fluid, and very dark in color. The brain was congested, and the lateral ventricles full of serum. The liver, lungs, and kidneys were also congested, but otherwise healthy.

There was no inflammatory or corrosive appearance of the mucous membrane. The author believes that if the stomach-pump had been efficiently used within a short time after the accident, the fatal issue might have been avoided. R. H. Quill (*Jour. Royal Army Med. Corps*, Oct., 1903).

Case of acute poisoning with quinine in a child of 16 months. She had taken 4.5 Gm. (70 grains) of quinine bisulphate in the form of sugar-coated pills or confections which had been left accidentally exposed. Half an hour later she was pale, restless, refused food, and complained of abdominal pains. Her hands grew cold and on the way to the hospital she was taken with convulsions and vomiting. On admission she was in a state of collapse, with occasional general tonic-clonic contractions of the muscles, subnormal temperature, loss of consciousness, general hypoaesthesia, mydriasis, loss of the light reflex, and absence of the radial pulse. She vomited repeatedly in the hospital and died two and a half hours after taking the drug, in a state of coma. No special lesions were found in the organs at autopsy. Federici (*Rivista di Clinica Pediatrica*, May, 1906).

Case of poisoning by quinine in a little girl of 18 months, who had received quinine hydrochloride in doses of 20 cg. (3½ grains) daily. She took from 6 to 8 tablets of quinine by accident on one occasion (1.2 to 1.6 Gm.—19 to 25 grains). After fifteen minutes she was taken with convulsions, tremor, loss of consciousness, vomiting, cyanosis, and diarrhea. The respiration became of the Cheyne-Stokes type, the pulse was thready, the reflexes were abolished, and the child died. Groseff (*Archives de méd. des enfants*, vol. x, 1907).

Case of a soldier who, having a little fever, took 2 fluidounces (60 c.c.) of an "essence of quinine," amounting to about 240 grains (16 Gm.) of quinine. He died two and a

half hours afterward. It was not discovered that he was ill until an hour and a half after he had taken the dose, and for an hour afterward every effort was made to save him. The signs and symptoms present when he was first seen were: breathing stertorous, pulse barely perceptible, pupils equal but widely dilated, no corneal reflex, and the body cold and clammy. Director of the Medical Services in India (Jour. of the Royal Army Medical Corps, Sept., 1912).

**Treatment of Poisonous Effects of Quinine.**—**Atropine** has been recommended by Aubert to overcome the tinnitus induced by quinine. Others have found it useful in antagonizing the skin eruptions. Full doses of **hydrobromic acid** or **potassium bromide** will sometimes prevent both tinnitus and headache, especially if **ergot** be given in addition.

Report of 3 cases of neuralgia in which the author was able to reduce greatly and even suppress the tinnitus and other disagreeable symptoms due to quinine by the addition of small doses of atropine sulphate. From 5 to 7 grains (0.3 to 0.45 Gm.) of quinine were given at a time, and to each dose was added  $\frac{1}{40}$  grain (0.00046 Gm.) of **atropine** sulphate. In one case this prevented the untoward symptoms, and in the two others greatly moderated them. The periodical pains were delayed, and no appreciable degree of atropinism was experienced. P. Aubert (Lyon méd., Jan. 3, 1897).

The unpleasant cutaneous manifestations sometimes following the administration of quinine may be prevented by giving 15 drops (1 c.c.) of the tincture of **belladonna** or  $\frac{1}{40}$  grain (0.001 Gm.) of atropine with each dose. Astrop (Old Dominion Med. Jour., Feb., 1905).

Tinnitus caused by quinine can be quieted by compression of the vertebral arteries. This has the effect of diminishing the pressure in the

basilar artery, its branches in the internal auditories, and thereby in the vessels of the labyrinth. The compression may be made in the suboccipital region, the thumb and finger of one hand being placed in the hollows behind the mastoid process while counterpressure is made by the other hand on the forehead. As the arteries lie under the complexus muscle the pressure must be rather firm. Dundas Grant (Journal of Laryngology; Medical Record, Dec. 8, 1906).

Case of threatening acute malaria in which the necessary quinine caused convulsions with fever whenever it was taken. After disastrous trials of various preparations of quinine, the patient was placed under the influence of **morphine** and **atropine**. Quinine up to 15 grains (1 Gm.) was then injected without further disturbance, promptly arresting the threatening symptoms. Nogara (Gaz. degli Osped., Sept. 20, 1908).

In the presence of delirium, **morphine** is likely to be useful. Where circulatory and respiratory depression appear, the stimulating measures usually employed in such an emergency are indicated.

Large doses of **morphine sulphate** recommended as the antidote for quinine. When the toxic symptoms of quinine are apparent—dilatation of the pupil, with vision disturbed, deafness and ringing in the ears, power of locomotion partly lost, and general depression of all faculties, heaviness of the head, and drowsiness—the author gives  $\frac{1}{2}$  grain (0.032 Gm.) of morphine sulphate at bedtime and repeats this every day until all symptoms have disappeared. Large doses of morphine counteract quinine, while small doses supplement its toxicity. J. Y. Shearer (N. Y. Med. Jour., Dec. 21, 1907).

In severe quinine intoxication the author gives tonics for the heart and kidneys, rejecting ergot, however, because he believes that it "tetanizes"

the kidney function. Matarazzo (Gaz. degli Osped., May 24, 1908).

Case of a man 40 years old, six feet tall, weighing about 225 pounds. Had been a hard drinker. Not feeling well, he had taken 2 tablets of bromoquinine (containing about 5 grains—0.3 Gm.—of quinine). In about half an hour he began to feel short of breath and his skin became very red. At first there were small white elevations about the size of a pinhead, very close together, and with very red skin between. Two hours after he had taken the quinine, he was very red all over; face swollen; lips, nose, veins of forehead, and finger-nails, blue; pupils dilated widely, and conjunctivæ congested. He complained of dyspnea and at times would ask to be put close to the window, although the window was raised up high close to the head of his bed. At times he seemed delirious. The pulse was quite impalpable, and the heart sounds inaudible. His feet were cold, as was his entire skin. Nitroglycerin,  $\frac{1}{400}$  grain (0.00065 Gm.), under the tongue;  $\frac{1}{100}$  grain (0.00065 Gm.) digitalin hypodermically; 20 drops (1.25 c.c.) of aromatic spirit of ammonia, repeated in twenty minutes; and a tablet of strychnine, atropine, and digitalin produced no apparent change in the condition. **Camphorated oil** (3 grains—0.2 Gm.—in 30 minims—1.85 c.c.—of olive oil) was then injected into the leg; in fifteen minutes the pulse began to return at the wrist, and in half an hour the man felt about all right again. He was given a purgative, and later was seen sitting up and reading the paper. The redness of the skin was all gone. This man gave a history of two similar attacks caused by quinine. H. W. Sherwood (Amer. Jour. Clin. Med., July, 1912).

#### **THERAPEUTICS. In Malaria.**—

This is the most important therapeutic application of quinine, which ranks as a specific in practically all forms of malarial disturbance. Jancso, Rosen-

berger, and others have shown that when the drug is given four to six hours before a malarial paroxysm the number of parasites in the blood is markedly reduced in from one to three hours. *In vitro* quinine in a 1:10,000 solution is found to inhibit at once the ameboid movements of the plasmodium, and even a 1:20,000 solution proves very poisonous to them. When the drug is taken into the infected human system there may occur a preliminary increase in the movements of the parasites; but this is followed after a time by diminished activity. The plasmodium shrinks, becomes granular, and finally disintegrates.

A point of diagnosis between **malarial fever** and other febrile diseases of the tropics lies in the fact that the former always yields, even at a selected time, to a single dose of quinine properly administered, while the latter do not react in this way. M. E. Legrain (La presse méd., July 7, 1900).

Quinine acts most strongly upon the organisms that are breaking up into spores and upon the spores themselves, while its effects are least marked after the spores have definitely established themselves in fresh erythrocytes. Since the period of spore liberation corresponds in time with the malarial chill, the administration of quinine before a paroxysm will not prevent the latter, as it will meet the organisms when they are most refractory. The spores, however, will be largely destroyed by the drug as they are set free, and the succeeding chill thus more or less diminished in intensity, according to the completeness of destruction of the parasites. In view of the fact that some of the young parasites may escape the action of the drug, it is considered advisable by some not to depend on a



single dose, however large, as this will soon be eliminated, but to keep the blood continuously supplied with quinine through hourly doses, so that the parasites may be exposed to its effects both a short time before the paroxysm and for a number of hours after it. It is hardly justifiable to administer the drug during the paroxysm itself, as it tends to aggravate headache and favors vomiting. (This does not apply to pernicious forms of the disease.) Certain observers, however, have advised the administration of 10 or 15 grains (0.65 or 1 Gm.) of quinine during the period of sweating, or after the paroxysm is entirely over, and a like dose five hours before the time at which the next paroxysm is due. They contend that the most powerful parasiticidal effect is obtained in this way, *i.e.*, by single large doses. It is to be remembered, of course, that where the sulphate of quinine is used the drug will not be very rapidly absorbed; the maximal concentration of quinine in the blood will occur only some three to six hours after its ingestion, and the effect obtained if the drug is given during the decline may not be as good as if it had been administered at a slightly earlier period in the cycle. It is therefore advised by most authors to give the drug some hours before an expected attack. In any case, if the drug as taken at the initial paroxysm fails to prevent the appearance of the succeeding one, another full dose should be given, preferably in solution, as soon as the preliminary symptoms appear.

Use of cinchona recommended in cases where quinine fails to act. The author has cured several malarial patients by substituting the entire drug for the abstracted alkaloid. Two Gm. (30 grains) of cinchona being equiva-

lent to 25 cg. (4 grains) of quinine, the dose must be eight times as large. Zilgien (*Jour. des prat.*, Sept. 8, 1906).

In the intermittent form of malaria the author gives 10 to 30 grains (0.65 to 2 Gm.) of quinine sulphate on retiring, and 10 grains (0.65 Gm.) in the morning; this is modified often in proportion to the severity of the condition, but less than 10 grains (0.65 Gm.) is never given. During the daytime spirit of nitrous ether is given every three or four hours with water. In the remittent form he at once gives 30 or 40 grains (2 or 2.6 Gm.) on retiring, repeats on the second day with from 20 to 30 grains (1.3 to 2 Gm.), and so on, until the remittent form is converted to the intermittent form, when the treatment already cited is applied. J. Y. Shearer (*N. Y. Med. Jour.*, Dec. 21, 1907).

A larger proportion of the drug is destroyed by the organism when administered in a single large dose than when it is given in divided doses in the course of the day. This would suggest that a better action is obtainable when the drug is used in a large single dose, as recommended by Robert Koch, than when it is given in divided doses. It is to be remembered, however, that the plasmodium, when subjected to fractional doses, comes in contact with the quinine for a longer time than in the opposite case. The proportion of the drug destroyed in the organism is larger when it is used hypodermically than when it is given by mouth. Giemsa and Schaumann; translated by Chatterjee (*Calcutta Med. Jour.*, April, 1909).

Pyretic phase in action of quinine described. Experiments showed that if the drug is given too soon either it has no action or the pyretic phase of the quinine influence will be superposed on that of the malaria. Given too close to the paroxysm, the quinine does not have time to manifest its antipyretic action. The sensitized organism is liable to react with the

febrile phase, and the febrile condition is magnified through combination of the malarial and quinine pyrexias. In the subcontinuous form of malaria, lacking the control of the thermic cycle, if quinine is given routinely, it may induce continued high temperature from the thermic reaction to the quinine by the soil sensitized by the malaria. A single dose of 1 to 2 Gm. (15 to 30 grains) of quinine should be given a few hours before the paroxysm. S. Mircoli (Gaz. degli Ospedali e delle Clin., May 17, 1908).

In the administration of quinine the aim should be to have the blood saturated with the drug just when the attack is expected. This is accomplished by giving the usual dose of 1 Gm. (15 grains) fractioned in five doses, the last being taken just two hours before the anticipated attack. The same amount is taken on the day between the attacks, and after they have subsided smaller amounts are continued for a few days. All of 120 cases were cured by two applications of quinine according to the above rule. When a large dose is given at one time, about half of it is promptly eliminated, leaving only the other half to combat the parasites. A much smaller proportion is eliminated early when fractional doses are used. Palumbo (Gaz. degli Ospedali, Sept. 2, 1909).

Where a particularly prompt effect on the part of quinine is desired the drug may be given by intramuscular injection, in the form either of the hydrochloride of quinine and urea or of quinine bishydrochloride or hydrochlorosulphate (*v. Modes of Administration*). Intravenous injection may also be availed of in the severe cases.

A number of physicians living in the malarial districts of the South were requested for information as to their experience with the hypodermic use of quinine. In the main the replies showed a confidence in the method. When the quinine is dissolved in normal salt solution and is

not too concentrated—about 10 grains (0.65 Gm.) to  $\frac{1}{2}$  ounce (15 c.c.)—then the results are good. When the solution is concentrated or has an acid reaction, the results are *nil*. Twenty grains (1.3 Gm.) of quinine hydrochloride and urea and 1 pint (500 c.c.) of normal salt solution is an excellent mixture. The writer has used the intravenous method three times with good effect. Administration by the rectum is very unsatisfactory. J. B. McElroy (Memphis Med. Monthly, Nov., 1902).

Method of using quinine hypodermically in India described. Either the hydrobromide or bisulphate is used. The former is the more soluble salt, but the latter is possibly the more powerful, and is soluble in warm water in the proportion of 1 grain (0.065 Gm.) in 4 minims (0.25 c.c.) of warm distilled water. This is warmed before use by placing the bottle containing the solution for a few minutes in  $\frac{1}{2}$  cupful of hot water. The dose usually given to an adult is 5 grains (0.3 Gm.), but for men of large stature 10 grains (0.6 Gm.) are not excessive in a severe attack. Ten grains (0.6 Gm.) may be used for any adult if the fever refuses to fall with the smaller doses. Osler uses 30 grains (2 Gm.), but the author has never had a case requiring such a dose.

The skin of the part to be operated on is disinfected with mercury bichloride or phenol. The back of the upper arm or flank is the best place to choose.

The next step is to wash out the syringe repeatedly with hot water and smear the needle with carbolized oil. The solution is then injected quickly into the subcutaneous tissues, avoiding, of course, important vessels or nerves. The bleb formed under the skin should be at once dispersed by gentle friction with a finger smeared with carbolized oil. If this precaution be not taken a painful lump will be left at the seat of injection, which will remain there for months. When done as thus de-

scribed the hypodermic injection of quinine is hardly more painful than that of morphine; indeed, it is very often absolutely painless. Care must be taken not to inject the quinine endermically.

Quinine thus used is more efficacious, dose for dose, than when administered by the mouth. Praises lavished on solitary injections, however, can only be the outcome of a very limited experience. Thus in one of the author's cases daily injections of 5 grains (0.3 Gm.) for five consecutive days had no apparent effect on the course of the fever; the drug was then administered in 5-grain (0.3 Gm.) doses thrice a day by the mouth for five more days and the fever disappeared. Smyth (Brit. Med. Jour., Nov. 15, 1902).

The parasite of malaria is susceptible to a minute proportion of quinine. When the drug is swallowed more is found in both the blood and urine than when it is injected under the skin. But experience has shown that the latter method of administration is more efficacious in malaria. This is due to the prolonged action of the drug in this case, as it passes continually, though slowly, from the tissues into which it has been injected to the blood. Luca (Archives Ital. de Biol., March, 1905; Brit. Med. Jour., July 1, 1905).

In the estivoautumnal type of malaria, the parasites are often more refractory to quinine than in the tertian or quartan forms. This applies particularly to the crescent stage of the organism. The cycles of development are, moreover, less regular than in the other types, and the febrile attacks more prolonged. It is, therefore, more necessary in this form that a continued quinine effect be exerted on the parasites, and this is done by giving small doses at intervals, *e.g.*, every four hours.

It is generally recommended that a cholagogue cathartic, such as calomel,

be given before the administration of quinine, the action of which is thereby favored. In alcoholics, the giving of 1 grain (0.06 Gm.) of capsicum with each dose of quinine is useful to hasten the absorption of the latter. It is also stated that where large doses of quinine are used the effects of the drug on the brain may be largely avoided by combining morphine with it.

The blood in malaria is less alkaline than normal. A preliminary administration of sodium bicarbonate enhances to a marked degree the action of quinine. In all but 2 out of 27 cases of continuous malarial fever the fever was arrested by this procedure within two days. Economou (Grèce méd., vol. v, No. 23, 1905).

After the violence of the malarial paroxysms has been overcome by means of quinine, given as already explained, the drug should be further administered at definite intervals to prevent a relapse, one full dose of 10 or 15 grains (0.6 or 1 Gm.) being given every seventh day, beginning from the time of the last paroxysm, for a period of one or two months. Arsenic may be given during this time with advantage, in order to favor repair of the injury done by the disease.

In the remittent or "bilious" forms of malarial fever, where due to the estivoautumnal parasite, quinine should be pushed with greater vigor than is necessary in the more benign intermittent type of the disease. If administration by mouth fails to give satisfactory results, the intramuscular or intravenous route should be resorted to. In the milder cases where the tertian or quartan plasmodia may be causative, the drug should be given for a few days in full doses every six or eight hours, or in hourly doses of 2 to 4 grains (0.12 to 0.25 Gm.). Rest in bed,

with a fluid but thoroughly supporting diet, and careful attention to the bowels—calomel is frequently used—are also important measures in cases of the remittent type. The quinine should always be given in a readily absorbable form, *e.g.*, in solution in aromatic sulphuric acid (1 drop to each grain). Warburg's tincture (*v.* Preparations and Doses) has given good results in remittent malaria. In the severe cases, as they occur in the tropics, Steudel warns against the use of small doses of quinine, which tend to aggravate the trouble, while large doses are specific.

Comparative study made in over 100 cases of tropical malaria between the customary method of administering quinine, *i.e.*, giving the drug when the temperature returns to 37° C. (98.6° F.), and that advocated by Nocht, which consists in giving 0.2 Gm. (3 grains) of quinine hydrochloride five times daily at two-hour intervals for a week. To avoid recurrence, in Nocht's method, the drug is continued for two or three months, in periods of two days each, separated by pauses of increasing length,—two days at first, then three, then four, etc., up to eight, which is not exceeded. The results obtained with the two methods appeared identical as regards lowering of the fever, rapidity of disappearance of parasites from the blood, and avoidance of recurrences. The Nocht method, however, proved advantageous in reducing to a minimum the disagreeable by-effects of quinine, as well as in affording greater certainty of escaping hemoglobinuric fever. Werner (*Therap. Monats.*, March, 1911).

In the pernicious forms of malaria, prompt and repeated intravenous administration of full doses is advisable. Where this is not feasible, 30 to 75 grains (2 to 5 Gm.) should be given by the mouth, by the rectum, and subcutaneously, in divided doses within

twelve hours. In addition, symptomatic treatment is required on account of the condition of the gastrointestinal tract, nervous system, kidneys, and lungs, any or all of which may need attention.

In malarial cachexia with more or less profound anemia, quinine is generally of but little real value, except for the purpose of preventing relapses of febrile paroxysms and as a stomachic bitter (Rosenau and Anderson). Iron, arsenic, and laxative mineral waters are especially indicated in these cases.

The value of quinine in hemoglobinuric (blackwater) fever appears to depend largely upon the presence or absence of parasites in the blood. It is believed by a majority of observers that this affection is often due to the malarial infection itself, but others have clearly shown that quinine is capable of inducing hemoglobinuria in malarial patients previously free from it. The correct procedure to follow, therefore, in these cases is to examine the blood for estivoautumnal parasites in the ameboid condition (the crescentic form is refractory to quinine). If the parasites be found, quinine may be cautiously given; if not, or if those found consist exclusively of crescents, its use is valueless, and may do harm. In those cases in which the hemoglobinuria appears in direct association with the malarial attacks, the administration of the drug is, of course, plainly indicated for the purpose of preventing further paroxysms. According to J. H. Sears, hemorrhages are apt to follow the ingestion of quinine in malaria when the action of the kidneys is partially or completely suppressed. In all instances, rest in bed, calomel, great care to avoid chilling of the skin surface, and the taking of warm liquids are important features of the treatment.

Case in which there was doubt as to the diagnosis between pernicious malaria with jaundice and hemoglobinuria and Tomaselli's disease, which is an intoxication with quinine giving rise to fever, hematuria, jaundice, three or four hours after the administration of quinine. A subcutaneous injection of quinine showed no benefit after two hours; on the contrary, the fever increased, and the urine became more bloody. Three days later the patient of his own accord took 30 cg. (5 grains) of quinine bisulphate. Within a few hours he developed chills, vomiting, marked jaundice, and pains in the loins. The urine became black, the temperature rose, and the pulse increased. The quinine was immediately stopped, and saline irrigations of the colon were ordered, with the result of abating the symptoms in a short time. The dose of quinine does not influence the gravity of the symptoms in these cases. Therefore, a subcutaneous injection of quinine should be given in order to distinguish them from pernicious malaria. If Tomaselli's disease is present, the symptoms will increase in severity, while in true pernicious malaria they will abate, and quinine may then be continued. *Festa (Gaz. degli Ospedali, Feb. 7, 1904).*

Persons who react to quinine with serious hemoglobinuria and other alarming symptoms are able to tolerate effectual doses if the drug is administered by the hypodermic route. The author has observed cases of serious quinine intoxication in persons free from malaria. In one instance the entire train of symptoms of threatening quinine intoxication occurred spontaneously in an attack of malaria; no quinine had been taken for a month. *Matarazzo (Gaz. degli Osped., May 24, 1908).*

Upon administration of quinine by rectum, even when an easily soluble salt is used, the absorption is distinctly less than by mouth. Insoluble quinine salts are unsuitable for rectal use.

In the case of **blackwater fever**, the quantity of quinine excreted was found, on an average, larger than otherwise, and the excretion extended through a larger number of days. This permits of the conclusion that the condition originates as a consequence of the fever and not through the decomposition of quinine and the action of some poisonous element separated from it by the organism. *Giemsa and Schaumann; translated by Chatterjee (Calcutta Med. Jour., April, 1909).*

In various nervous conditions associated with chronic malarial intoxication, *e.g.*, hemicrania and variously situated neuralgias, quinine given in doses of from 1 to 6 grains (0.06 to 0.4 Gm.) every two to six hours will often afford great relief. The same is sometimes true of choreic or epileptic manifestations, asthma, spasm of the larynx, hiccough, or other motor disturbances which may occur periodically in malarial subjects.

Finally, as a prophylactic measure in those exposed to malarial infection, the administration of quinine has yielded excellent results. The amount to be given is ordinarily from 3 to 6 grains (0.2 to 0.4 Gm.) daily, though this had better be doubled in regions where the incidence of the disease is high. The drug is also often taken at longer intervals.

Observations made for five weeks in Corsica on 35 vintagers, each receiving 0.7 Gm. (11 grains) every third day. Only one attack occurred in a woman, of slight severity. The method of living was favorable to infection. In preceding years one-third or one-half had been attacked. The author prefers the hydrochloride to other salts. No gastric irritation, headache, or buzzing in the ears was observed from this dose, although 0.8 Gm. (12½ grains) had previously been found to cause the last two

effects. J. Michon (Arch. gén. de méd., June 23, 1903).

The chief methods of administering quinine for purposes of prophylaxis are: (1) Koch's method of 1 Gm. (15 grains) of quinine on each of two consecutive days at intervals of ten days; (2) Plehn's method of 0.5 Gm. ( $7\frac{1}{2}$  grains) given every fifth or every fourth day; (3) 1 Gm. (15 grains) given once a week, or two doses of 0.5 Gm. ( $7\frac{1}{2}$  grains) given on two consecutive days once a week, and four doses of 0.1 to 0.25 Gm. ( $1\frac{1}{2}$  to 4 grains) given every day. Only 4 of 41 Europeans under observation in New Guinea followed Plehn's method, and no definite conclusion as to it could be arrived at. Two out of the 4 had each an undoubted attack of malaria while under treatment. One Gm. (15 grains) of quinine given once a week, or 0.5 Gm. ( $7\frac{1}{2}$  grains) twice a week, does not protect from malaria. Eight persons followed Koch's method; two had no attack while taking quinine, one for ten months, another for four months, and a third had one slight attack only in fifteen months; a fourth remained well for four months, but then discontinued the use of quinine, and promptly sickened with malaria. In applying Koch's method, the author would give the quinine every eighth and ninth day, or every ninth and tenth day, after consideration of the individual case. It should be given an hour before a meal, that is, when the stomach is empty. Koch's method has no injurious effect upon an otherwise sound organism. It will greatly contribute to diminishing the prevalence of blackwater fever. Wendland (Arch. f. Schiffs- u. Tropen- Hygiene, Bd. viii, Heft 10, 1904).

Answers supplied by 59 persons living in German East Africa to questions as to the efficacy of a prophylactic use of quinine showed that none of the recognized ways of taking quinine prophylactically gives an absolute protection against malarial infection, nor even against an out-

break in cases in which the disease is latent. Individual condition, especially with respect to the state of the gastrointestinal tract, is a factor of great weight. Other factors are locality, the prevalence of malaria among the natives, the number of anopheles, etc. That if the exposure to infection be long enough continued no form of quinine administration will prevent malarial infection appeared from the fact that of 8 persons not previously infected only 1 had an attack during three months of quinine prophylaxis, but of 7 who continued the prophylaxis for a longer time 4 had an attack.

The ordinary method of quinine prophylaxis—taking 1 Gm. (15 grains) of quinine on the ninth and tenth days—in all but a few cases gives rise to unpleasant symptoms; sensitive persons are rendered unfit for work for the greater part of the day. Moreover, the sensitiveness to quinine tends to increase, and in many cases the absorption of quinine is hindered by weakness of the digestive organs. The method should be modified, where necessary, to reduce the side-effects to a minimum, and where the liability to infection is prolonged mechanical protection against mosquitoes should be resorted to if possible. Meixner and Kudicke (Arch. f. Schiffs- und Tropen- Hygiene, Nov., 1905).

Quinine hydrochloride given in cachets or gelatin capsules is the best form of administration for prophylactic purposes. In general, the dose should not be less than 1 Gm. (15 grains), and it is only in people who suffer severely from the side-effects that it may be diminished or the hydrochloride replaced by 1.5 Gm. (24 grains) of equinine. In most localities adequate protection is given if the quinine be taken every eighth and ninth day. The dose is best given, if convenient, in the morning before breakfast, when the absorptive powers are most active. The keeping of a quinine calendar, in which the days for taking quinine are

clearly marked, is advisable. A specially stringent prophylaxis is needed for native troops. Morgenroth (Archiv f. Schiffs- und Tropen-Hygiene, Bd. x, Nu. 5, 1906).

Administration of quinine for the production of immunity in persons exposed to malarial infection cannot absolutely control an epidemic, but is beneficial among troops and prisoners. It will decrease the number of malarial cases by from 50 to 80 per cent. at the most, when the dose is given regularly and in an adequate manner; it will also decrease the gravity of the cases. Acton (Indian Med. Gaz., Aug., 1910).

#### As Antipyretic in Other Disorders.

—The antipyretic action of quinine is best obtained from doses of 15 to 30 grains (1 to 2 Gm.), given in the course of an hour. It has been utilized for the reduction of temperature in **typhoid** and **typhus fevers**, but at best its action is weaker than that of the coal-tar drugs, and these, in turn, have been largely superseded by the use of cold baths. Some have used quinine in smaller amounts— $7\frac{1}{2}$  to 9 grains (0.5 to 0.6 Gm.), divided into two doses given at an eight-hour interval—with the aim of retarding the combustion of body tissues and wasting resulting from the continued fever in typhoid. Jaccoud advises its use in cases where the morning remissions in the fever are but slight, or in which the evening temperature persistently exceeds  $40^{\circ}$  C. ( $104^{\circ}$  F.); he gives  $22\frac{1}{2}$  to 30 grains (1.5 to 2 Gm.) on the first day, 15 to  $22\frac{1}{2}$  grains (1 to 1.5 Gm.) on the second, then allows two days' rest before the drug is resumed. In any event, quinine should be used with caution in typhoid patients whose heart shows signs of weakening; small doses are then alone permissible (Manquat).

As is the case with the other antipyretic drugs, the most marked effects on the temperature are obtained when the latter has already begun to fall, or the patient has been treated with cold baths.

Quinine given as a powder suspended in milk. In the first series of observations the temperature began to fall within forty-nine minutes; in the second series within twenty minutes, and in the third series within twenty-two minutes. The size of the dose within certain limits—20 or 40 grains (1.3 or 2.6 Gm.)—does not seem to affect the rapidity of the defervescence. The antipyretic effects of the quinine are probably due to the production of diaphoresis. William Sykes (Brit. Med. Jour., Nov. 3, 1900).

The activity of quinine, both as antimalarial and antipyretic, is augmented by combining it with aromatics, cholagogues, and moderate amounts of alcohol, and herein lies the secret of the famous "Warburg tincture." Its antipyretic action may be further augmented by giving it in conjunction with (1) remedies which relax the peripheral capillaries, as the powder of ipecac and opium, and (2) remedies which exert a definite antifebrile effect through an action upon the nerve-centers, as acetanilide, antipyrin, etc. The combination of quinine with Dover's powder may well be administered in capsules or cachets, and the constipating effect of the opium may be overcome by small doses of resin of podophyllum or calomel. In combining quinine with acetanilide, a fluid mixture is preferable, of which the following is a good type:—

*R* Quinine sulphate,  
Acetanilide (in fine  
powder) ..... 3j (4 Gm.).  
Aromatic elixir (or  
elixir of Calisaya) ..... f3j (30 Gm.).  
Chocolate syrup  
q. s. ad ..... f3iv (120 Gm.).  
Dose: 1 to 2 teaspoonfuls.

(The syrup of chocolate should be heavy—similar to that drawn at soda-water fountains.)

It has also been found that the action of small doses of quinine is augmented and sustained by combination with other cinchona alkaloids. The following combination is of particular value, 3 grains (0.2 Gm.) being equal in antipyretic effect to at least 2 grains (0.12 Gm.) of quinine sulphate:—

R Quinine sulphate,  
Cinchonine sulphate,  
Cinchonidine salicylate .....ãã gr. xxx (2 Gm.).

Mix. Divide into 30 capsules. Dose: 1 to 3 capsules.

(The powder should not be made into a mass, but after the ingredients have been well mixed together they should be put directly into the capsules, and the capsules weighed as made up.) J. H. Egbert (Merck's Archives, Oct., 1900).

In **yellow fever** and in the hectic fever of **pulmonary tuberculosis**, quinine has also been used in doses of 2 or 3 grains (0.13 to 0.2 Gm.), given every two hours.

**In Various Inflammatory and Suppurative Affections.**—Quinine is used with more or less success in a large variety of conditions to antagonize inflammatory changes and exert a general stimulating effect on the organism. Although not a specific antagonist to bacterial pullulation as it is to the malarial plasmodium, quinine may, perhaps, in some measure act as an auxiliary to the body in overcoming bacterial infections. It has been shown, moreover, by H. Lyon Smith that moderate doses of quinine exert a favorable effect on phagocytosis.

Researches made to confirm or disprove the statement that quinine, like alcohol in excess, inhibits phago-

cytosis, and is therefore contraindicated in septic conditions. The opsonic index was taken as a basis for the work. It was calculated that a 10-grain (0.65 Gm.) dose of the acid hydrochloride of quinine given to a person weighing 140 pounds, if entirely absorbed, would represent in the blood a proportion of 1 to 7500. The influence of this amount on the phagocytosis of different kinds of pathogenic organisms (streptococci, staphylococci, pneumococci, *B. coli*, *B. influenza*, *B. pseudodiphtheriae*, and *B. tuberculosis*) was contrasted with stronger and weaker solutions to ascertain the effect of varying doses. In the majority of the experiments there was an increased phagocytosis, always most marked with the 10-grain (0.65 Gm.) dose solution. Smaller doses were less effective, and very large doses (30 and 40 grains—2 and 2.6 Gm.), instead of increasing, actually diminished phagocytosis, sometimes to the extent of 50 per cent. Smith (Lancet, Nov. 5, 1910).

In acute catarrhal inflammations of the air passages, quinine is frequently used with advantage. Thus, in **acute coryza**, 10 grains (0.6 Gm.) of the drug, combined with Dover's powder, opium, or morphine, will, if given early, often avert the attack. It may also be used as a 0.2 per cent. spray. Similarly, 10 grains of quinine given at the beginning of an attack of **acute tonsillitis** will sometimes abort the disease or prevent pus formation.

In **influenza** quinine has given good results, and even been regarded by some as a specific. It should be given in doses of 8 grains (0.5 Gm.) daily, and is especially useful for mucous-membrane inflammation where this is the chief feature of the disorder. Huchard advised giving 1 Gm. (15 grains) on the first day or two of the disease, but such a dose is permissible only where asthenia is slight or



absent. Allbutt uses  $\frac{1}{2}$ - to 1- grain (0.03 to 0.06 Gm.) doses of quinine in combination with digitalis in the treatment of cardiac poisoning in influenza. Burney Yeo advises the use of quinine after two or three days' preliminary treatment with salicin. He gives the former in doses of 1 to 3 grains every three or four hours, either in a solution of citric acid or in lemon juice. Beard counsels the employment of euquinine in influenza, in preference to any of the official preparations.

In **whooping-cough** quinine is used both internally and externally. Great benefit has been derived from it in some instances, though a number of authors prefer antipyrin for routine use. Baron advises that quinine be used in doses of  $1\frac{1}{2}$  grains (0.1 Gm.) for each year of the child's age, which are to be administered 3 times daily, at 6 A.M., 2 P.M., and 10 P.M. The dose corresponding to five years should not be exceeded, even in older children; otherwise, disturbances of hearing may result. According to Hamill, quinine is beneficial only in the later stages of chronic cases, in which doses of from 3 to 9 grains (0.2 to 0.6 Gm.) daily tend to arrest the coughing spells. (For best methods of giving quinine to children, see section on Modes of Administration.) Externally, the use of quinine is recommended by Henke and Hare, who spray the fauces and pharynx every few hours with a 0.2 to 0.4 per cent. solution, and believe that transmission of the disease to other children is thereby hindered. Since it is the posterior portion of the tongue which is most sensitive to bitter tastes, it may be necessary to paint this area with a 1 per cent. solution of cocaine in order to facilitate the use.

of this measure. Binz has given quinine hydrochloride hypodermically in cases where the drug was not tolerated by the mouth.

In an epidemic of **whooping-cough** the writer found that the disease seemed to be aborted in every case in which quinine was given in large doses systematically for several days in succession, and the drug retained. The pertussis was of an unusually serious type. The author has always found exceptional tolerance for quinine in children, no appreciable disturbances having been noted in a number of children in an endemic focus of malaria who took by mistake, for malaria, 6 and 7 Gm. ( $1\frac{1}{2}$  to  $1\frac{3}{4}$  drams) of quinine bisulphate. For pertussis he does not hesitate to inject in the course of a day 0.5 Gm. ( $7\frac{1}{2}$  grains) of acid quinine hydrochloride for infants and 1 Gm. (15 grains) for children up to the age of 5. On cessation of the tendency to vomit he gives the drug by the mouth and continues it for eight or ten days, by which time the disease has usually completely subsided. F. Andalo (Policlinico, July 4, 1909).

Whooping-cough treated by applying to the nasal mucous membrane a salve containing 1 to  $2\frac{1}{2}$  Gm. of quinine in 10 to 15 Gm. of lard (*i.e.*, 30 grains to 2 drams in the ounce). A portion of salve the size of a pea was introduced into each nostril three or four times daily by means of a glass rod, and caused to pass back in the nasal cavities by lowering the child's head. In general, the symptoms were considerably improved at the end of three or four days. The frequency and severity of the paroxysms were decreased, and the characteristic whoop was soon lost, the cough becoming of the usual type. The method is especially effective in very young children. L. Berliner (Münch. med. Woch., Feb. 15, 1910).

In **hay fever** quinine is extensively used. Kyle advises the administration, in cases where ordinary treat-

ment fails to relieve the irritation caused by the nasal secretions, of a pill containing 2 grains (0.12 Gm.) of quinine hydrobromide,  $\frac{1}{200}$  grain (0.0003 Gm.) of atropine, and  $\frac{1}{8}$  grain (0.008 Gm.) of codeine, which is to be taken 3 times daily. In **asthma** quinine has sometimes been used as an antipyretic and restorative tonic after the severity of the paroxysm has abated.

In various forms of bronchial or pulmonary inflammation, this alkaloid is asserted to give good results. Thus, in **chronic bronchitis** with profuse secretions it has been recommended, and in the **bronchopneumonia** occurring in association with measles has been advised for the purpose of retarding or preventing cheesy degeneration of the lung. In **lobar pneumonia** occurring in children a favorable influence is exerted by 2 grains (0.12 Gm.) of quinine given 3 times daily.

In the corresponding condition in adults large doses of quinine, *e.g.*, 20 to 40 grains (1.3 to 2.6 Gm.), given during the congestive stage and before exudation has occurred, are held, notably by S. Solis-Cohen, to exert a limiting, if not an abortive, influence on the disease.

In **pneumonia** the author gives 10 to 30 grains (0.65 to 2 Gm.) of quinine sulphate at noon, since the temperature curve rises so characteristically toward evening; this is followed with a large dose, 30 or 40 grains (2 or 2.6 Gm.), on retiring. Repeatedly, though not invariably, the crisis is forestalled, and convalescence at once follows. In severe cases where the first application of this measure fails, it is repeated, and almost always the crisis is passed by lysis before the ninth or eleventh day. J. Y. Shearer (N. Y. Med. Jour., Dec. 21, 1907).

Pyogenic infections of various kinds are not infrequently distinctly inhibited by the use of large doses of quinine. Thus, in **septicemia**, **pyemia**, **puerperal fever**, the stage of suppuration in **small-pox**, **endocarditis**, **perinephric abscess**, and allied conditions the internal administration of 5 to 20 grains (0.3 to 1.3 Gm.) every four hours will in a certain proportion of cases bring the inflammatory process to a standstill. Wherever abscesses are present quinine tends to reduce the discharge and prevent generalization of the infection.

In **erysipelas** quinine may be given alone in doses of from 5 to 10 grains every four hours, or in smaller doses (2 to 5 grains, or 0.12 to 0.3 Gm.) in combination with tincture of ferric chloride (10 to 20 minims, or 0.6 to 0.12 c.c.).

In **tropical splenomegaly** (kala-azar) quinine appears to have been productive of some benefit, though it is more useful for purposes of prophylaxis. In **relapsing fever** it is sometimes capable of interrupting the series of successive febrile paroxysms, while in the **spotted fever** of the Rocky Mountains full doses, given hypodermically, have been thought to exert some favorable effect on the course of the affection (Rosenau and Anderson).

A very marked decrease in the leucocytes is always found in uncomplicated cases of **cachexial fever** associated with the Leishman-Donovan bodies, and when they number below 2000 per c.c. this is almost diagnostic of the disease, though it may rarely occur in true malarial cachexia. They are reduced to a greater degree than the reds, so that the ratio falls below 1 to 1000 in all uncomplicated progressive cases. This is rarely so in true malarial cachexia. Red-marrow

tabloids are of great value in increasing the leucocytes. High remittent fever is accompanied by progressive deterioration of the blood and general condition, but it may be often to a large extent reduced to the less injurious intermittent form by continued large doses of quinine, combined with red marrow. The best results yet reported have been obtained by those who carry out vigorous quinine treatment. Leonard Rogers (*Brit. Med. Jour.*; Treatment, Oct., 1905).

In **syphilis** the author adds quinine sulphate to the regular specific treatment, the dosage depending upon the stage of the disease, thus: primary stage, 10 grains (0.65 Gm.) three times a week for two months, then twice a week for four months; secondary and tertiary stages, 10 grains (0.65 Gm.) every evening for one month or six weeks; then twice a week for four months. In this way he alternates during the entire specific treatment with quinine sulphate for six months and rest for an equal intervening period. By this means the usual systemic depression is avoided. J. Y. Shearer (*N. Y. Med. Jour.*, Dec. 21, 1907).

Treatment of **syphilis** with quinine revived. The author injects intravenously  $\frac{1}{2}$  Gm. ( $7\frac{1}{2}$  grains) quinine hydrochloride, repeats this dose the next day, then injects 0.6 Gm. ( $9\frac{1}{2}$  grains), and repeats the latter injection four times at four-day intervals. By the ninth injection, all symptoms vanish. He used about 5 Gm. (75 grains) quinine hydrochloride in the course of from fourteen to twenty days, and believes that this treatment may prove useful where mercury fails or is not well tolerated. Lenzman and Knapp (*Boston Med. and Surg. Jour.*, Nov. 19, 1908).

**Acute rheumatism** and related sub-acute or chronic states, including **lumbago** and **myalgias**, were formerly often treated with quinine, which is not without beneficial effect in these

conditions, though far inferior to salicylic acid. The salicylate of quinine may prove useful, though its use in large doses would seem unsafe, owing to the possibility of a cardiac depressant effect. Briquet, using quinine in rheumatic fever, prescribed it in progressively increasing amounts, up to 45 grains (3 Gm.), but always gave fractional doses, so that the patient never received more than  $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 Gm.) at a time. Small tonic doses of quinine—1 to 2 grains (0.06 to 0.12 Gm.)—may prove useful in rheumatism after the pain has subsided. In rheumatic pericarditis with effusion, quinine has been used apparently with benefit.

Quinine salicylate used with favorable results in **rheumatism**, **diphtheria**, **influenza**, **pneumonia**, **enteric fever**, the **infectious diseases** generally, and **chlorosis**. In acute rheumatism it may be substituted with great advantage for sodium salicylate in 5-grain (0.3 Gm.) doses thrice daily, given in cachets, after the first few days of the disease. It is less depressing than the sodium salt. In diphtheria it is valuable in doses of 3 to 5 grains (0.2 to 0.3 Gm.) thrice daily. In typhoid fever the drug seems to be far superior to phenyl salicylate or any of the so-called intestinal disinfectants, the invaluable salicylate of bismuth not excepted. Given early in the disease, perhaps after a moderate dose of calomel has scavenged the intestinal canal, and continued throughout the fever or even into convalescence, the drug has appeared to regulate the bowels, correct the fetor of the evacuations, check tympanites, and control any tendency to vesical catarrh; the fever runs a mild and favorable course.

In a sharp attack of **herpes zoster**, quinine salicylate relieved pain and seemed to play successfully the part of a tonic. John Moore (*Practitioner*, Jan., 1903).

**As Bitter Tonic and General Stimulant.**—Tonic effects are obtained with quinine given in doses of  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 Gm.) three times daily. The drug not only acts as a simple bitter, but appears to stimulate, to a certain extent, the nervous system in general, and is, in addition, claimed by some to increase the number of red blood-corpuscles.

Quinine acts, according to the dose used, (1) as a tonic, (2) as a stimulant, (3) as an antipyretic or depressant. The tonic action is produced by doses of from  $\frac{1}{2}$  grain to 1 or 2 grains (0.032 Gm. to 0.065 to 0.13 Gm.). In doses of from 3 to 5 grains (0.2 to 0.3 Gm.) every three or four hours the action is distinctly that of a stimulant. There is a stimulating action upon the heart and the entire vascular system. As an antipyretic quinine sulphate should be given in doses of from 10 to 40 grains (0.65 to 2.6 Gm.). J. Y. Shearer (N. Y. Med. Jour., Dec. 21, 1907).

Small doses of quinine have a favorable effect on the blood, even when long continued. The proportion of hemoglobin was found increased in dogs, as also the number of red corpuscles, and an active leucocytosis of polynuclear cells was observed. The daily dose of quinine (given subcutaneously) approximated 0.4 Gm. (6 grains) for each 70 kg. (154 pounds) of weight; this is the dose generally given by the mouth in the prophylaxis of malaria. When the daily dose was larger than this an injurious influence on the blood soon became apparent. D. de Sandro (Riforma Medica, March 7, 1910).

Among gastric conditions in which its bitter tonic effect is utilized are **chronic gastritis, chronic gastric dilatation, carcinoma of the stomach, gastric atony** (motor insufficiency), and **anorexia nervosa**. Both increased secretion and motility are obtained through its action. Cinchona prepa-

rations, especially the compound tincture, are generally used in preference to the alkaloid in these conditions. Thus, Kemp recommends the following combination as stomachic:—

℞ *Tinct. nucis vomicæ*,  
*Acidi hydrochlorici*  
*diluti* ..... āā f3iij (12 c.c.).  
*Tinct. cinchonæ comp.* f3ss (16 c.c.).  
*Aquæ destillatæ*. q. s. ad f3iv (125 c.c.).

M. Sig.: One to 2 teaspoonfuls in a wineglassful of water half an hour before meals.

In various conditions associated with depression of nervous functions, such as **neurasthenia, neuralgias** (especially periodic), and **general debility**, including that present during convalescence from acute diseases, tonic doses of quinine are useful. Similarly, when prolonged mental or physical strain is to be undergone, 2 to 4 grains (0.12 to 0.25 Gm.) daily will tend to support the system and prevent exhaustion.

In the eruptive fevers—**scarlatina, measles, small-pox**—quinine in small, frequently repeated doses is useful where there is adynamia, and in larger doses at longer intervals may prove of some value in controlling excessive pyrexia. The same applies to cases of **diphtheria**.

The **night-sweats of pulmonary tuberculosis** are sometimes favorably influenced, it is said, by tonic doses of quinine. The effect on the appetite is also likely to be of value.

Jaboulay and Launois appear to have found quinine of some value in inoperable **cancer cases**. They give 15 grains (1 Gm.) by the mouth five days in each week, on the other two days substituting Fowler's solution. Where gastric disturbance is produced, subcutaneous administration is resorted to (Manquat).

In **angioneurotic edema**, **intermittent hydrops of the joints**, and **Raynaud's disease** good results appear to have sometimes been obtained from the use of quinine.

Certain conditions associated with disturbance of the brain-centers have been advanced as indicating the use of quinine, and may be supposed to bear some relation to the evident physiological effects of large doses of this alkaloid on the brain and organs of special sense. Thus, in **delirium tremens** tonic doses of quinine are said to be of value in quieting the patient, although this appears to apply chiefly to cases where marked general enfeeblement is present. In persons of advanced age the drug may afford relief from such symptoms as vertigo and headache, as well as from amnesia and melancholic tendencies, probably by improving the blood-supply to the nerve-centers. In **Ménière's disease** Charcot claimed that the daily administration of 9 to 12 grains (0.6 to 0.8 Gm.) of quinine for two weeks, followed by an intermission of equal duration, would bring relief if persisted in, though the first few doses might cause temporary aggravation.

Remarkable effect produced by quinine, even in small doses, in cases of **labyrinthine vertigo**, referred to. The results of the author's studies seem to show that the sensibility of the internal ear is generally diminished by the drug. Dundas Grant (Ninth Internat. Cong. on Otol.; Rev. hebdomadaire de laryng., d'otol., etc., Oct. 19, 1912).

In **chorea** H. C. Wood suggested the use of large doses of quinine, having found that intravenous injection of the drug in choreic dogs caused prompt cessation of the spasmodic movements. Clinically, the

measure proved of great value in a certain proportion of cases, though these appeared to be chiefly the cases in which the drug was tolerated in considerable doses. Potts found that **incontinence of urine** was in some cases similarly overcome by large doses.

Animals treated with quinine found to endure a dose of strychnine double or triple that endured without quinine. In cases of **strychnine poisoning** heroic doses of quinine should be employed, as these undoubtedly exert a favorable influence. Valdés Dapena (Revista de Med. y Cirur. de la Habana, Oct. 25, 1903).

In **diabetes mellitus** Lécorché found that a daily dose of 5 to 7½ grains (0.3 to 0.5 Gm.) given for a week or two is capable of lowering the sugar excretion almost to one-half its previous level, and believes the drug to be useful even in the absence of any nervous disturbance. Frerichs, on the other hand, considers quinine useful only for the attendant headache and neuralgic pains elsewhere (Manquat).

**As an Oxytocic and Emmenagogue.**—Quinine has been used in the treatment of **uterine inertia**, though it is not very efficient. In spite of former assertions, it is now generally conceded that quinine alone is incapable of producing abortion. According to Cadwallader, quinine will excite the already acting uterus because of its general stimulating effect, but has no specific action in initiating uterine contractions.

In nervous or hysterical patients who have a tendency to abort, however, it may be best, in giving full doses of quinine, to combine it with a sedative,—for example, bromides or opium.

Quinine does seem occasionally to exert abortifacient properties. One woman induced abortion three times by taking quinine in daily doses of 30 to 75 grains (2 to 5 Gm.). On becoming pregnant the fourth time she also took quinine, but, as it did not produce the desired effect, she repeated the quinine every month at the time of expected menstruation, for three months, without success. At the fourth month she took 120 grains (8 Gm.) of quinine, and abortion took place on the day following. F. Schwarz (Klin.-therap. Woch., S. 1464, 1900).

Schwab asserts that the oxytocic effect of quinine appears in twenty to thirty minutes after its ingestion. He gives it in two doses of  $7\frac{1}{2}$  grains (0.5 Gm.) each, administered at an interval of ten minutes. It is indicated when the uterine contractions are insufficient during the period of cervical dilatation, or where, the membranes having ruptured, delivery must be hastened. Mackness uses 4-grain (0.25 Gm.) pills of the sulphate, two being given to begin with, and a third, if necessary, an hour later. He holds that quinine does not induce tetanic contraction of the uterus, but merely increases the strength of the labor pains, while allowing complete relaxation between them. Nonetheless, quinine should not be given where there is any mechanical hindrance to delivery, such as disproportion between the fetus and the pelvis. According to some observers, the use of quinine is attended with a slight increase in the tendency to severe post-partum hemorrhage.

In labor and in cases of simple uterine inertia, quinine excites intermittent and frequent uterine contractions, exactly similar to normal pains and entirely different from the tonic contractions following the adminis-

tration of ergot. The author has found the drug especially valuable in multiparæ where after the beginning of labor the pains are slow and weak and the os well dilated. The exhibition of 16 grains (1 Gm.) of quinine will in such cases produce after fifteen to thirty minutes stronger and more frequent pains, which will often rapidly terminate labor and obviate the use of forceps. In primiparæ the drug proved less valuable, probably because here the slowness of labor is due to failure of the head to engage rather than lack of nervous energy. The objection that quinine may cause severe post-partum hemorrhage has not been borne out by the author's experience. Neither has he observed cinchonism. M. H. Fussell (Therap. Gaz., Jan., 1901).

Quinine used as oxytocic in 66 cases. When it acts at all it seems to be more effectual than any other drug. Conitzer (Archiv f. Gynäk., Bd. lxxxi, F. v. Winckel Nu., 1907).

Quinine advised to increase uterine contractions during labor, and even sometimes to initiate them. It is particularly useful where the membranes have ruptured prematurely, and the contractions are absent or feeble. It was also employed in the induction of premature labor and in the treatment of abortion. No injurious effect on either mother or child was observed, the ringing in the ears sometimes noted soon passing off. The author administers 1 Gm. (15 grains) by the mouth in a cachet, giving half the quantity one hour after and again in half an hour if required. He has not found it of any use to exceed 2 Gm. (30 grains). It has generally answered very well to give it by the mouth, although in some cases recourse was had to subcutaneous injection. The author has never known it to fail. Maurer (Brit. Med. Jour., Dec. 14, 1907).

Case of a woman who had been bleeding profusely from some uterine cause. Prompt relief was obtained by 40 grains (2.6 Gm.) of quinine sul-

phate. **Hemorrhages** of whatever nature, post-partum especially, may be checked by the administration of quinine sulphate in large dosage. Small doses, on the other hand, increase hemorrhage. J. Y. Shearer (N. Y. Med. Jour., Dec. 21, 1907).

In **amenorrhea** quinine may be used in small doses to stimulate the menstrual flow. It will also increase the lochial discharge.

Quinine is very useful in congestive **dysmenorrhea**, by diminishing the flow of blood to the genital organs, and in dysmenorrhea due to neuralgia. It may also prove useful in **amenorrhea**, by stimulating the contraction of the uterus and of the utero-ovarian vessels, which would in their turn stimulate the dormant ovulation. In **metrorrhagia** and **menorrhagia** not dependent upon any organic disease, it is very effective. The author gives the quinine in doses of 8 to 24 grains (0.5 to 1.5 Gm.), and he combines it with digitalis or ergot, as may seem indicated. Dalché (Presse méd., Jan. 8, 1901).

**In Cutaneous Disorders.**—In many skin diseases—**acne**, **ecthyma**, **erythema nodosum**, **dermatitis herpetiformis**, **herpes zoster**, **pemphigus**, etc.—small daily doses of quinine are beneficial.

Case of a woman of 46 years who had suffered for twelve years from repeated attacks of **erythema nodosum** which resisted all medication, including intravenous injections of sodium salicylate. Hydrochlorosulphate of quinine was then injected intravenously on alternate days for three weeks. The erythema nodosum later reappeared, but there was no more fever, and the general condition, previously serious, remained permanently good. The author often uses intravenous injections of quinine in rheumatism when salicylates fail; intramuscular or subcutaneous injections do no good in these cases. In neuralgias, including sciatica, where

morphine fails to relieve, the procedure also gives excellent results in a certain proportion of cases. Soca (Jour. des maladies cutanées, May, 1908).

Good results obtained in a case of **lupus vulgaris** which had already recurred three times after Finsen-light treatment by the following procedure: A 1.5 per cent. solution of quinine sulphate in distilled water, acidulated with 1 drop (0.06 c.c.) of sulphuric acid to each 10 Gm. (2½ drams) of the solution, was exposed for two hours to direct sunlight, or for four hours to diffused light, or, again, in winter, for two hours to an electric arc. The fluid thus obtained, containing absorbed light rays, was injected daily with a fine needle through the healthy skin margins surrounding the involved areas into and under the diseased tissues. In four to ten days the skin of the parts treated became detached, leaving ulcerations 3 or 4 mm. deep, lined with reddish granulation tissue. Dressings of "illuminated" solution proving too irritating, an "illuminated" 10 per cent. ointment of quinine sulphate was applied instead. In the third to the fifth week after treatment a scar was formed over the area, in most instances not depressed below the surrounding surface, and deep infiltrations disappeared. Control injections in the same case with a quinine solution prepared and kept in the dark were found to be without influence on the progress of lupus. T. Brinch (Semaine médicale, Sept. 18, 1912).

**Locally as Antiseptic and Astringent.**—Quinine possesses pronounced antiseptic properties, and has been used externally as a dressing to **wounds**, **ulcerations**, etc. According to Alfödi, in infected wounds showing no disposition to heal, treatment with a 1 per cent. solution of quinine sulphate exerts a prompt cleansing effect and leads to a more rapid recovery than where a dressing of mercury

bichloride or iodoform is used. This applies also to uninfected wounds.

Quinine tried as a substitute for iodoform, with great satisfaction. A solution containing quinine hydrochloride 1, alcohol 3, and distilled water to 100 parts was used. The quinine may be increased to 2 or more per cent. As a styptic, gauze soaked in one of the above solutions is without equal in **bleeding** from the parenchyma of organs such as the liver. As a disinfectant it **infected wounds** and **sinuses**, it is efficient and certain. The solution is also a convenient means of freeing the hands from infective matter during an operation. H. Marx (Centralbl. f. Chir., Nov. 9, 1901).

Quinine lygosinate found experimentally to possess marked antiseptic power. The drug was used as a powder for dusting on wound surfaces, for impregnating gauze and other dressings, for suspension in glycerin, and finally for combination with the gum on adhesive plaster. A thin layer of the powder, dusted on, was used in many cases of **unclean wounds**, in foul, **gangrenous conditions**, and the like. It acted as a deodorant and an antiseptic, so that the secretions soon became harmless, odorless, and only slightly purulent, while the whole wound showed healthy granulations. **Ulcerating cancer** also was deodorized and dried by means of the powder. In cases of **bone disease** a 10 per cent. suspension of the drug in glycerin was injected into the wounds or the powder itself rubbed in, with similarly successful results. **Sinuses** and **fistulæ** yielded to it, and **bleeding**, especially oozing from the parenchyma of organs, was easily checked with it. It is not poisonous, because so little of it is absorbed. J. Hevesi (Centralbl. f. Chir., Nu. 1, 1902).

Mixture of 1 dram (4 Gm.) of quinine with 8 ounces (250 c.c.) of codliver oil (to be shaken well before use) employed with good results in **tertiary syphilitic** and **rheumatic**

**ulcers**, ordinary **ulcers**, **gangrene** of the **skin**, **burns** in which large surfaces had sloughed away, and other similar conditions. All wounds took on a healthy appearance. In **intertrigo** the effects of the preparation are good, if it is not too long continued. For **eczema** it does not act well, unless at the same time gastric troubles are corrected. J. Read (Lancet, Feb. 15, 1902).

Antiseptic power of quinine tested against *B. pyocyaneus*, *Staphylococcus aureus*, *B. anthracis*, and *B. mesentericus vulgatus*. The two former were killed in from thirty to sixty minutes by a 1 to 1.5 per cent. solution, while a 1.5 to 2 per cent. solution killed the sporulating micro-organisms in twenty-four hours. The action, therefore, is more potent than that of phenol or formaldehyde, and deserves a place between these and corrosive sublimate; a  $\frac{1}{4}$  to  $\frac{2}{3}$  per cent. solution of quinine salts produces agglutination phenomena with bacteria, while when added to blood a very marked agglutination of the red cells can be observed. Quinine applied locally is capable of arresting **bleeding**. The formula used is: Quinine hydrochloride, 5 Gm. ( $1\frac{1}{4}$  drams); alcohol, 15 Gm. (4 drams); water, to make 150 Gm. (5 ounces). A tampon saturated with this solution is applied to wounded surfaces; also in cavities. A half-minute is sufficient to arrest bleeding.

The author has also devised a 1 per cent. quinine gauze similar to iodoform gauze, but odorless; its formula is: Quinine, 5 Gm. ( $1\frac{1}{4}$  drams); alcohol, 15 Gm. (4 drams); water, 170 Gm. ( $5\frac{2}{3}$  ounces), and gauze, 500 Gm. (16 ounces). When employing a packing of wet quinine gauze, it is unwise to leave this *in situ* for over twenty-four hours, since the coagulation of albumin renders a prolonged use dangerous. H. Marx (Münch. med. Woch., April 22, 1902).

Report of 6 cases of **uterine prolapse** treated by injections of quinine sulphate into the broad ligaments. In 1 there was recurrence; in the other



5 a cure was obtained. Two of these 5 subsequently bore children, without a return of the prolapse. The quinine injections occasionally caused slight fever and malaise, but no abscess or other untoward results were produced. Davidson (Brit. Med. Jour., Aug. 3, 1912).

In **subacute** or **chronic cystitis**, irrigation of the bladder with a weak solution of quinine will tend to prevent decomposition of the urine. In **gonorrhea** the use of quinine solutions has frequently been recommended. In the acute stage solutions of about 0.05 per cent. strength may be used; later 1 or 2 per cent. solutions will be applicable, exerting a more marked astringent effect. Jullien advises the use of the following injection in cases of gonorrhea in which ordinary measures have failed to cure:—

℞ *Quinina sulphatis* ..... gr. xv (1 Gm.).  
*Bismuthi subnitratis* ..... gr. lxxv (5 Gm.).  
*Acaciae* ..... ʒiiss (10 Gm.).  
*Glycerini* ..... fʒj (30 Gm.).  
*Aquæ destillatæ bulliatæ* ..... fʒiiiss (100 Gm.).—M.

Quinine bisulphate, 1:3000 to 1:1500 solution as daily irrigation will cure at least 50 per cent. of cases of **acute gonorrheal urethritis** in two weeks. It is less irritating than potassium permanganate solutions, is anesthetic, tonic, and strongly antiseptic. In preparing the solution it is best to dissolve the quinine in a glass of very hot water and then add this to the irrigating syringe filled with warm water. If there is still a residue, the solution should be filtered. A. E. Mowry (Old Dominion Med. Monthly, Sept., 1912).

In nasopharyngeal infections a 0.5 per cent. spray of quinine may prove useful.

Internally, the antiseptic and astringent properties of quinine are made use of in **amebic dysentery**, **cholera Asiatica**, **cholera infantum**, and in the yeasty vomiting resulting from the growth of *Sarcina ventriculi* in the stomach.

In the first of the above affections quinine is employed for rectal irrigation, with excellent results. A solution of 1:3000 strength is sufficient to destroy amebæ, but stronger solutions, up to 1:500, are also used. In cholera Fullerton advised the use of quinine both as a therapeutic measure and for prophylactic purposes. At the beginning of the attack he gives 15 to 20 grains (1 to 1.3 Gm.) within two hours.

Quinine is frequently used as an ingredient of hair tonics. The following preparation has been suggested by Brinton for use in **alopecia**:—

℞ *Quinina sulphatis* . gr. lxxx (5.2 Gm.).  
*Tincturæ capsici*,  
*Tincturæ cantharidis*,  
*Spiritus ammoniæ aromatici* ..... āā fʒss (15 Gm.).  
*Alcoholis*,  
*Glycerini* ..... āā fʒiv (120 Gm.).  
*Aquæ* ..... q. s. ad Oj (480 Gm.).

M. Sig.: To be well rubbed in locally.

**As Local Anesthetic.**—For this purpose the double hydrochloride of quinine and urea is practically alone of value among the quinine salts, although Griswold as early as 1896 and Chavenne more recently have reported fairly satisfactory results from other salts of quinine, either alone or combined with other local analgesic substances.

Following formula employed in **operations upon nose and throat** in children or individuals who show an idiosyncrasy toward cocaine:—

℞ *Phenolis*,  
*Mentholis*  
 āā ..... 2 Gm. (30 grs.).  
*Quinina*  
*hydro-*  
*chloridi* . 1.5 Gm. (24 grs.).  
*Adrenalin* . 0.005 Gm. ( $\frac{1}{12}$  gr.).—M.

This forms a syrupy fluid, to be applied in small amounts. Cauterizations and small operations can be performed without pain. The combination is not caustic, since menthol counteracts the caustic properties of phenol. The presence of quinine considerably increases the anesthetic effect, though quinine alone was unsatisfactory. Chavenne (Klin.-therap. Woch., Dec. 12, 1910).

The quinine and urea compound is made by dissolving quinine hydrochloride in hydrochloric acid, adding pure urea, filtering the mixture through glass-wool, and allowing it to crystallize. Its anesthetic action is due, according to the researches of McCampbell, to coagulation of the protoplasm of the peripheral nerves. The drug was found capable of causing temporary paralysis, and in large doses atrophy, of the extremities in the animals experimented upon.

This agent being freely soluble in water, any desired strength of solution can be used, though, with the exception of cases where a surface anesthesia of mucous membranes is desired, and a 10 to 20 per cent. solution is therefore employed, solutions ranging in strength from 0.25 to 4 per cent. are most commonly used. In 2 to 4 per cent. solutions the drug appears to exert a decided hemostatic effect, especially as regards the capillaries, whereas in 0.25 or 0.5 per cent. strength little or no such action is apparent, and the addition of a small amount of epinephrin is by some considered desirable. There is

a certain tendency to induration of tissues when the salt is used for infiltration, but this nearly always disappears in the course of a few weeks or months.

The induration and thickening which is caused by quinine and urea hydrochloride, instead of being cellular, is due to a purely fibrinous exudate. Apparently nearly all of this is later absorbed. With a 0.25 per cent. solution this induration does not occur to any notable degree, and this strength is advisable in operations where speedy primary union of the skin is desirable and where anesthesia lasting more than several hours is desired. Hertzler, Brewster, and Rogers (Jour. Amer. Med. Assoc., Oct. 23, 1909).

Quinine and urea hydrochloride in 1 per cent. solution used in cases of **anal fissure** and **hemorrhoids**. The amount necessary was 45 to 80 minims (2.8 to 5 c.c.); distention of the tissues necessary in all cases. Anesthesia, more or less complete, began in four to twenty-three minutes, and lasted from twenty-four hours to nine days. Capillary bleeding was much reduced; arterial and venous, not controlled, possibly reduced. Induration appeared in 3 cases in ten minutes to one hour and continued from five to twelve days. Normal sensation returned in twenty-four hours to twelve days. Hyperesthesia for sensation was present in 2 cases; in 1 hemorrhoidal case it lasted twelve days. W. Green (Jour. Amer. Med. Assoc., June 11, 1910).

There was some induration in the majority of cases in which the author used quinine and urea hydrochloride, but at the end of three months this had disappeared in nearly all of them. The drug had a very decided hemostatic effect. Some cases have been reported in which it was successfully used in major operations. W. A. Boyd (Med. Record, Oct. 14, 1911).

Recent experience has shown that quinine and urea hydrochloride can

be substituted for cocaine in nearly every operation for which the latter has commonly been used. Its two great advantages are: 1. Low toxicity; the difference in toxic power between cocaine and the quinine salt may be expressed by a ratio of at least 40 to 1. No constitutional effects need be feared from free use of the quinine compound, except in individuals with a marked idiosyncrasy. 2. Long duration of the local anesthesia; according to Boyd, the average is three days, while Thibault places it at four or five hours. This is claimed to be a marked advantage in cases where pain is likely to persist for some time after the conclusion of the operation, *e.g.*, in the removal of hemorrhoids.

Case of strangulation of an old **inguinal hernia** in a woman aged 64 who had, in addition, inoperable cancer of the uterus and rectum. The circulation was poor. The operation was done under local anesthesia, induced by injecting a 0.25 per cent. solution of, quinine and urea hydrochloride. The tissues above the canal were moderately infiltrated with the solution, and there was no pain until after the canal was laid open, when the peritoneum was found to be quite sensitive. About 2 drams (8 Gm.) of the warmed solution were poured into the canal and in a few minutes there was perfect anesthesia of the parietal peritoneum and the operation was finished without the patient at any subsequent time feeling any pain, although considerable adhesions were broken up. There was no local peritoneal reaction, union was primary, and there was no shock. Henry Thibault (Jour. Amer. Med. Assoc., April 23, 1910).

Quinine and urea hydrochloride causes only slight local irritation. It does not cause tissue destruction, and, if it interferes with healing at all, does so only to a slight degree. It is

especially valuable in all local operations where a large amount of anesthetic will be necessary, as **fistula in ano**, **hemorrhoids**, **rib resection for empyema**, etc. In many cases there is a slight momentary pain as the first few drops of the solution are injected. This disappears almost instantly and no further sensation is experienced. The anesthesia is very lasting. Suturing the wound never hurts, as it often does when cocaine has been used. It should not be used intravenously for anesthetic purposes. H. F. Graham (L. I. Med. Jour., June, 1910).

Numerous **operations on the nose**, **superficial tumors**, and other lesions in mucous membranes performed under local anesthesia with quinine and urea hydrochloride. The method did not prevent local hemorrhage, oozing recommencing at the slightest excuse when the dressings were changed. The anesthesia induced is more strictly localized than with cocaine and lasts longer; the compressing dressings could be renewed five hours later without pain. The reduction of sensibility persisted on an average fully three days. Cicatrization seemed to be a little retarded, the wound not healing quite as quickly as with cocaine. The absence of vasoconstriction may interfere a little with the operation; addition of epinephrin may obviate this, although it was the author's impression that the latter in combination with the quinine had a less intense vasoconstricting action than alone. Gaudier (Presse méd., July 2, 1910).

Quinine and urea hydrochloride is a valuable and safe local anesthetic. Anesthesia may be obtained in from three to forty-five minutes; in the majority of the author's cases it was complete in ten minutes. It is as profound as with cocaine, eucaïne, or novocaine, and of much longer duration, lasting from a few hours to several days. Bleeding is not controlled by the drug, though it is materially lessened, especially by the use of the stronger solutions. In

none of the cases in which **intranasal operations** were done did it become necessary to pack the nostrils. In none of the cases of **amygdalectomy** did the patient miss a meal, the act of deglutition causing no pain. Solutions ranging in strength from 1 to 4 per cent. were used. In general, in cases where primary union is to be obtained it is desirable to use the lower percentages, though sometimes, in vascular areas, the stronger solutions may be employed without materially delaying union. W. Green (N. Y. Med. Jour., May 6, 1911).

The salt has been used with satisfaction in operations in the anorectal region, on the tonsils, in turbinectomies and septal spur operations, as an anesthetic intravesical injection previous to cystoscopy, for the removal of encapsulated, benign tumors, such as lipomas, and also to some extent in aural work. It is recommended that in infiltration anesthesia at least ten to twenty minutes be allowed to elapse for the effect of the drug to appear.

Quinine and urea hydrochloride can be used with absolutely no ill effects in 0.25 per cent. solutions. The writer operated on a **fibrolipoma** of each shoulder, one the size of a hen's egg, the other the size of an orange. The dissection of the latter took one hour, the patient feeling no pain. In another case, one of rectal fistula, an ounce (30 Gm.) of a 1 per cent. solution of this drug was injected into the rectum, the patient holding it for about twenty minutes. A small amount of 0.25 per cent. solution was injected into the fistulous tract. F. M. McCartney (Denver Med. Times, April, 1910).

Technique of use of quinine and urea hydrochloride in **anorectal surgery** as practised by the writer is as follows: The anus and perineum are shaved and scrubbed with liquid antiseptic soap, then washed with a 1:1000 solution of iodide of mercury,

which is washed off with sterile water, and a compress of alcohol applied. At a point one-half inch below and posterior to the posterior commissure of the anus a spray of ethyl chloride or a drop of pure phenol is usually applied. Wherever possible, the index-finger, protected by a finger-cot and well lubricated, is inserted in the anus and the sphincter pulled downward and backward. The syringe contains about 1 dram (4 Gm.) of 1 per cent. solution of quinine and urea hydrochloride, and is armed with a fine sharp-pointed needle about two inches in length. The needle is inserted quickly, just underneath the skin, and 4 to 5 drops of the solution *slowly* injected. The point is then passed inward and laterally, going down toward and into the external sphincter muscle, which, guided by the finger in the rectum, is brought down toward the needle. The point should be kept about half an inch from the anal aperture, and the injection is carried up along the posterior lateral quadrant of the anus for about three-fourths to one inch. The needle is then retracted and pushed up on the other side, so that when the injection is completed the wheel of infiltration is U-shaped. Care should be taken lest the rectal wall be punctured. Three or four minutes are allowed to elapse for complete anesthesia to take place; then a vibrator is used to dilate the sphincter painlessly to a sufficient caliber to allow whatever operation is to be done. Many cases of **prolapsing hemorrhoids** can be operated upon without dilatation.

Substitution of quinine and urea hydrochloride for cocaine, gucaine, or other anesthetics is eminently satisfactory in all cases of rectal surgery where suturing of the integument is not required. Hirschman (Lancet-Clinic, July 9, 1910).

C. E. DE M. SAJOUS

AND

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**CINNAMON.**—There are several varieties of cinnamon, but the finest is the bark of the *Cinnamomum zeylanicum*, a small, evergreen tree, which is now almost exclusively a product of Ceylon. It is thin, smooth, and of light-brown color, having a highly fragrant odor, and a sweet, warm, aromatic taste. Cinnamon contains a volatile oil (*oleum cinnamomi*), tannic acid, mucilage, coloring matter, and lignin.

**PREPARATIONS AND DOSE.**—The following are the official preparations of the drug:—

*Oleum cassiæ* (oil of cassia or cinnamon). Dose, 1 to 5 minims (0.06 to 0.3 c.c.).

*Aqua cinnamomi* (cinnamon water), containing 0.2 per cent. of the oil. Dose,  $\frac{1}{2}$  to 1 fluidounce (15 to 30 c.c.).

*Spiritus cinnamomi* (spirit of cinnamon), containing 10 per cent. of the oil. Dose, 5 to 30 minims (0.3 to 2 c.c.).

*Tinctura cinnamomi* (tincture of cinnamon). Dose,  $\frac{1}{2}$  to 1 fluidram (2 to 4 c.c.).

*Pulvis aromaticus* (aromatic powder). This contains cinnamon, nutmeg, cardamom, and ginger. Dose, 15 grains (1 Gm.).

*Emplastrum aromaticum*, N. F. III (spice plaster). For external use.

**PHYSIOLOGICAL ACTION.**—Cinnamon is an aromatic stimulant, an astringent, and a hemostatic. It is also said to have antiseptic properties. Very large doses are soporific and cause death by failure of respiration.

**THERAPEUTICS.**—Cinnamon is commonly used as an adjuvant or to disguise the flavor of less agreeable drugs.

The spice plaster may be used as a counterirritant in **colic**, **neuralgia**, and **croup**. It is made by moistening the aromatic powder with hot whisky, and placing it between two layers of flannel.

The oil of cinnamon has been employed by some as a surgical dressing. Da Costa recommends the oil as injections in **gonorrhæa**.

Cinnamon may be used as a stomachic in **flatulency**, but is usually combined with other remedies. Relief may sometimes be obtained in **acute dysentery** by giving the powder in about 1-dram (4 Gm.) doses twice a day. It has also been used in passive **uterine hemorrhage**. J. C. Ross used large doses in the palliative treatment of **internal carcinomata**, believing

that it relieved the pain, decreased the odor, and gave general comfort. H.

**CIRCUMCISION.** See **PENIS AND TESTICLES, DISEASES OF.**

## CIRRHOSIS OF THE LIVER.

**—DEFINITION.**—The term “cirrhosis,” suggested by Laennec as a name for one particular condition of the liver, was not only found to be of immediate utility, but, like many other useful words, has rapidly acquired secondary meanings, and unfortunately the pathologist and the clinician disagree in the secondary meaning which they assign to the term. Hence a definition of “cirrhosis” satisfactory to all parties cannot well be given. The pathologist employs it to indicate *all those conditions in which there is a generalized, as opposed to localized or focal, development of increased amounts of fibrous tissue in the organ*; the clinician recognizes as included in the term *all those conditions characterized by connective-tissue overgrowth in connection with the liver, whether the overgrowth be focal or general, whether it affect the interior of the organ or the peritoneal capsule*, and urges in favor of this view that all these conditions may give rise to a like series of symptoms, while, on the other hand, he is unwilling to include under the terms such forms of connective-tissue overgrowth as give rise to no recognizable symptoms. According to this view, the gummatous liver of tertiary syphilis is cirrhotic, as is also the condition of chronic productive perihepatitis in which the capsule alone is affected, while the development of fibrous tissue in the centers of the lobules which may accompany chronic venous congestion of the organ is not to be classed as a cirrhosis.

Remembering that Laennec employed the word in association with a general-

ized fibrosis of the organ, and not to indicate the complex of symptoms induced by this condition, and recognizing, also, that it is impossible to restrict it nowadays to the one form which he described, the definition accepted by the pathologists more nearly approaches the original acceptation of the term, and will be adhered to in this article. At the same time, adequate reference will be made to such conditions as are not included in that definition, but which are regarded as cirrhosis by a large number of clinicians.

**CLASSIFICATION.** — Starting, then, with this definition, and including under the term all those states in which there is a generalized overdevelopment of connective tissue throughout the liver, it will be well, before attempting any classification, to pass in review the factors which primarily induce this overgrowth.

Our knowledge of the causes leading to fibrosis elsewhere, imperfect as it is, leads to the belief that inflammation is the main factor,—not acute, but, as it is termed, “productive.” It may be brought about by the action of a mild irritant extending over a relatively long period, or by the recurrent action of a somewhat more severe irritant. In either case there is a stimulus afforded to the proliferation of the connective-tissue cells of the part—and the new growth corresponds to the granulation tissue seen in a healing exposed wound. A prominent feature in fibroid tissue of this nature is its liability to contract. It would appear that in the commonest form of cirrhosis, the portal, or atrophic, this is the main process at work, the irritant reaching the liver by the portal vein and especially manifesting its activity by setting up an irritation along its interlobular branches.

This, however, is not the only form of inflammatory fibrosis. There may be a new development of connective tissue—a *replacement* fibrosis—to take the place of cells of a higher order, which, through the action of some irritant or disturbance, have undergone destruction, and it is still a matter of debate whether, in portal cirrhosis even, such replacement fibrosis is not largely concerned in the new growth. Sieveking, examining twenty atrophic cirrhotic livers by the Van Gieson method of staining, concluded that the connective-tissue growth was the first disturbance. Markwald came to the opposite conclusion: that necrosis of the peripheral liver-cells is the first event in the disease, and Ruppert describes both productive formation of connective tissues and inflammatory atrophy of the liver-cells. The more recent work of Opie and others upon the experimental production of cirrhosis demonstrates conclusively that degeneration of the parenchyma of cells is a factor of first importance.

In one form of cirrhosis,—the pericellular or interstitial,—of which in man the liver of congenital syphilis affords the best example, replacement fibrosis is the distinguishing feature. In this the various stages of cellular atrophy can be well followed, and the little groups of cells are to be seen surrounded by delicate new tissue of a character very different from that of the dense connective bands seen in portal cirrhosis. The difference makes itself evidenced by the gross appearance of the organ, for this form of fibrous tissue does not contract, the surface remains smooth, and the organ is enlarged instead of being diminished in size. It is significant that the contracting “portal” form of cirrhosis is asso-

ciated with the appearance of much elastic tissue in the new growth. It may be urged that enlargement of the organ is a proof of the productive character of the process, but the enlargement appears to be due, in the main, to a lack of pressure atrophy of the hepatic parenchyma so characteristic of portal cirrhosis, coupled with a compensatory proliferation of the liver-cells to replace those which have been destroyed. A proliferation or hypertrophy of this nature is occasionally well marked in the portal form, resulting in the formation of islands of new liver-tissue and the production of a "large hobnailed" liver. Rarely the new growth of the parenchyma advances to an adenomatous or even cancerous condition, and we meet with a greatly enlarged irregular cirrhotic liver with multiple neoplastic masses derived from the liver-cells.

If this process be the explanation of the hypertrophied liver of pericellular cirrhosis, the appearances in Hanot's cirrhosis present macroscopically and microscopically so many points of approximation to what has just been described that the fibroid overgrowth here may well be largely of the nature of a replacement fibrosis. The tendency is for recent observers to regard it as such, and to consider that biliary cirrhosis of the type which has especially been studied by Hanot is a cholangitis in which either the bile-capillaries within the lobule or the cells bordering upon these are especially affected. These liver-cells undergo gradual atrophy and replacement by new connective tissue. Goluboff regards this form as being primarily due to the chronic, diffuse, catarrhal angiocholitis with chronic, diffuse periangi-

ocholitis. Now, a catarrhal angiocholitis affecting the smallest bile-ducts affects the capillaries also, and is inevitably a process affecting the liver-cells themselves. But, while accepting these views with regard to the main characteristics of the fibroid changes of these two important forms of cirrhosis, it must, I think, be admitted that, save in relatively rare instances, the organs affected by one or other form of the disease show a mixture of both productive and replacement changes.

There are yet other ways in which fibroid tissues may be developed in various organs without recognizable inflammatory disturbance, and, as I have pointed out on more than one occasion, there may be increased development of fibrous tissue of a functional type. Such fibrosis is to be recognized in connection with altered conditions of the arterial, venous, and lymphatic circulation. It is difficult to say how far such forms manifest themselves in the liver. On the whole, the evidence is against there being any extensive development of new connective tissue in the organ from such a cause; but it may well be that the indurative form of passive congestion of the organ and the growth of fibrous tissue around the interlobular branches of the hepatic vein, in cases where there is long-continued obstruction of moderate degree brought about by either heart or lung disease, are to be regarded as due to a laying down of new connective tissue around the hepatic venules of non-inflammatory origin.

It is evident that, inasmuch as our definition is based upon the one condition of overdevelopment of fibrous tissue in the organ, a proper classification of the various forms of cirrhosis cannot be based primarily or adequately upon

the disturbances occurring in other parts of the body as secondary results of the hepatic fibrosis, but must be either etiological and made dependent upon the various causes leading to the development of fibrous tissue or, on the other hand, must—anatomically—be determined by the parts of the liver which are the primary seat of the development of the new tissue. Our knowledge of these cirrheses is still insufficient for either the etiological or the anatomical classification to be ideally perfect. Against the etiological classification it may be objected that what is regarded as the main etiological factor in the commonest form of cirrhosis—namely, alcohol—is not the direct cause of the condition. On the one hand, by far the commonest hepatic disturbance set up by alcohol is not cirrhosis, but fatty infiltration, and, on the other hand, identical cirrhotic conditions are found in the livers of certain confirmed alcoholics, and of little children and others who have never touched alcohol.

The mere enumeration of causes does not help us in every case to distinguish the special type of cirrhosis which those causes induce, the symptoms depending upon the form of hepatic disturbance. Such a classification can be of little clinical value.

It is evident also that the anatomical classification is imperfect to the extent that, while the disease may begin by affecting one special portion of the liver, as the process of fibrous-tissue development extends, it involves many other parts, and, consequently, in well-developed cases cirrhosis is anatomically of a mixed type, and it is far from easy in such cases to determine how the condition originated. The fullest etiological

classification is that given by Chauffard, and this has, at the same time, the advantage of being anatomical. He divides the cirrheses as follows:—

1. **Vascular** (originating around the vessels).

- |                |   |                                    |
|----------------|---|------------------------------------|
| (A) TOXIC      | { 1. Due to ingested poisons.<br>2. Due to autochthonous poisons.   |                                    |
| (B) INFECTIOUS | { 1. By the direct action of microbes.<br>2. By their indirect action through their toxins (or, as he terms it, tox-infection). | { (a) Local.<br>(b) Extra-hepatic. |
| (C) DYSTROPHIC | { 1. Arteriosclerotic.<br>2. Congestive.  |                                    |

## 2. Biliary.

- (A) DUE TO BILIARY RETENTION.  
(B) DUE TO ANGIOCHOLITIS OF THE SMALLER BILE DUCTS.

## 3. Capsular.

- (A) CHRONIC LOCALIZED PARIHEPATITIS.  
(B) CHRONIC GENERALIZED PERITONITIS.

Admirable as is this classification, it is difficult to see how we are to make the distinction which is here made between the toxic cirrheses and the tox-infective. Anatomically and clinically, poisons—whether absorbed from the stomach or developed in the system itself, or again passing into the blood as a result of the growth of micro-organisms, or again given off by micro-organisms within the liver itself—may produce similar lesions in the liver, and as a consequence bring about closely allied, if not identical, anatomical changes in the organ with the development of like symptoms. The distinction thus raised by Chauffard between these various forms is too fine for practical use; clinically, his subdivisions are almost valueless. For practical purposes we may recognize three or at most four main types of cirrhosis, and merely glance incidentally at certain other forms which are of interest to the pathologist rather than to the clinician. These main types are:—



**I. Multilobular Cirrhosis. Laennec's Cirrhosis, or Portal Cirrhosis.**—We have been accustomed to employ the last of these terms, but recent experimental studies to be presently noted throw doubt upon the previously accepted view that the process here shows itself necessarily first or mainly in immediate connection with the portal sheaths. It has not yet been absolutely established that the lesions produced in animals of the laboratory are identical with those seen in man; but certainly the mildest cases of cirrhosis in man (*e.g.*, often found associated with the fatty liver of the confirmed alcoholic) presents a small-celled infiltration and fibrosis of the portal sheaths and nothing more. But the irregular destruction and distortion of the hepatic lobules in more advanced cases are best explained on the assumption that there has been degeneration by no means confined to the cells at the periphery of the lobules.

**II. Unilobular Cirrhosis, Hanot's Cirrhosis, Infective Biliary Cirrhosis.**—In this the connective tissue is laid down with greater regularity around individual lobules with a tendency to infiltrate between the cell columns. The organ is greatly enlarged without hobnailing.

**III. Obstructive biliary cirrhosis,** due to obstruction of the larger bile-ducts. Here there is moderate enlargement.

**IV. Pericellular cirrhosis,** in man most often of syphilitic origin, and then most often due to the congenital, but occasionally seen in the acquired disease.

The other forms of minor importance are:—

**V. Arterial cirrhosis,** with periar-

teritis and development of fibrous tissue around the branches of the hepatic artery. Distinctly rare.

**VI. Centrilobular cirrhosis,** characterized by the development of fibrous tissue around the intralobular branches of the hepatic vein seen in some cases of long-continued passive congestion of the liver of moderate grade. Also rare.

**VII. Secondary cirrhosis,** due to extension inward of a chronic productive inflammation affecting the capsule of the organ. Some authorities describe this as occurring in the "zuckerguss leber," or "cake icing liver" of hyaloserositis. We have not encountered this type.

**VIII. Sporadic cirrhosis,** secondary to focal necroses scattered through the organ, or to development of inflammatory foci in no one well-defined portion of the liver-tissue, which act as centers from which there radiates fibroid change. The latter form is at times well seen in the liver of acquired syphilis around old gummatous areas. Of the former type the Japanese pathologists Fujinami and Yamagiwa (Nakamura Verhandl. d. Japanischen Pathol. Gesell., 1: 1911: 1) have described an excellent example in the cirrhosis of those affected by *schistosomiasis*. Like the allied bilharzia the adult *Schistosoma japonicum* lives in the mesenteric veins; its eggs are apt to be carried into the portal capillaries in the liver, there forming small emboli. Where these are few in number they cause little disturbance, although isolated nodules of granulation tissue are to be detected containing the eggs. But they may be so abundant as to set up a diffuse connective-tissue overgrowth (*hepatitis parasitaria embolica*).

The liver, at first enlarged, becomes contracted and nodular, with hobnailing coarser than that of the ordinary Laennec cirrhosis, not so coarse as that of the "hepar lobatum" of syphilis.

The writer has long favored the view that Laennec's cirrhosis is of an infective and not purely toxic nature. His studies upon a curious localized disease of cattle in Nova Scotia—then known as Pictou cattle disease, but since recognized also in New Zealand and South Africa—led him to believe that a member of the *B. coli* group was a factor in the causation. It is true that since then it has been amply demonstrated by Gilruth in New Zealand and Pethick in Canada that the disease is directly associated with eating fodder containing members of the *Senecio* family, and Cushny has obtained like symptoms by treating animals with the active principle isolated from one or other species of *Senecio*, although interestingly enough the *S. jacobaea*, the weed implicated in Nova Scotia, has given him no results. The author's view was that a gastritis, evidences of which were found in the affected cattle, permitted the entrance of the *B. coli* in excessive numbers into the portal circulation. He failed, however, to gain constant results when he inoculated his cultures into the animals of the laboratory. Hektoen and Weaver have, however, reported the production of typical cirrhosis in animals of the laboratory, the one by organism of the pseudodiphtheria group, the other by a member of the *B. coli* group, but here again we have reason to believe that the results ob-

tained cultivation the organisms lost their power of inducing cirrhosis.

There has been a similar striking inconstancy in the results obtained by those who have sought to induce cirrhosis by the administration of alcohol, phosphorus, chloroform, lead, and other drugs. It is unnecessary to detail the many experiments: suffice it to say that at times a true cirrhosis has been developed more often than the results have been negative.

[We owe to Opie (Trans. Assoc. Amer. Physicians, 25: 1910: 140) what is evidently the solution of the problem. Attention has been drawn of late years from many quarters (*e.g.*, Whipple and Sperring, Johns Hopkins Hosp. Bull., 20: 1909: 278; Howland and Richards, Jour. Exp. Med., 11: 1909: 344; Herter and Williams, Proc. Soc. Exp. Biol. and Med., 3: 1905: 23) to the fact that the prolonged administration of chloroform in man as in animals of the laboratory leads to a striking necrosis of the centers of the hepatic lobules. The cells of as much as three-fifths of the diameter of the individual lobules may be destroyed in this way. Here appeared to be an ideal method of inducing cirrhotic change. Opie found that, while he could produce the condition by feeding chloroform to his animals in small doses distributed over many weeks, prolonged anesthesia, while causing extreme necrosis, was recovered from without any increased fibrosis of the liver. There was complete regeneration of the liver-cells. Nor could he set up cirrhosis by sublethal doses of either the *B. coli* or the streptococcus. But now, when he combined the two processes, when, for example, he anesthetized a dog with chloroform and two or three days later gave an intravenous inoculation of a culture of *B. coli*, or when, again, he set up hepatic necrosis by the administration of small doses of phosphorus followed by inoculations of streptococci, in either case he obtained extreme cirrhosis of the multilobular type.

He has demonstrated thus that acute

death of the liver-cells is not followed by fibroid overgrowth, but that bacteria like the *B. coli* and the streptococcus, which, acting on the unaltered liver, produce no fibrotic inflammation, will surely induce cirrhosis if the vitality of the liver-cells be depressed. J. GEORGE ADAMI.]

If we may venture to apply Opie's results to ordinary so-called alcoholic cirrhosis in man, we may say that alcohol as such does not produce cirrhosis, but if, associated with the cell-depressant effects of the alcohol, there be a low form of infection, then cirrhosis is liable to be set up. And we may go further and say that the gastroenteritis set up by alcoholic drinks favors the excessive entry of forms like the *B. coli* from the intestinal canal into the portal circulation, and so that both directly and indirectly alcohol is capable of bringing about the action of the two factors which surely set up cirrhosis, namely, depressed state of the liver-cells, and what elsewhere I have termed subinfection. In support of this bacterial factor in ordinary cirrhosis is the not infrequent presence of indications of old inflammation extending from the liver—diaphragmatic and other adhesions; the presence of a right-sided pleurisy (suggestive of the extension of the inflammatory process through the diaphragm into the pleural cavity) and the frequent indications that the ascites is not purely mechanical, but is accompanied by a low form of inflammation.

Two cases of alcoholic cirrhosis of the liver in children, one of the patients being aged 16 months and the other 2 years and 11 months. Although there was an alcohol history in both cases, the alcohol had not been administered in excess. The first child had received wine, about a tablespoonful, twice a day, for eleven

months, for the purpose of strengthening its health. The second child, following an attack of whooping-cough, was given brandy, in doses of a dram (4 Gm.), twice a day, for about five weeks. Both patients did well under treatment. E. Jones (Brit. Jour. of Children's Dis., Jan., 1907).

Cirrhosis of the liver is met with seven times as frequently in the Calcutta post-mortem examinations as in those of Berlin. This great excess cannot be explained on the alcoholic theory of origin, for the disease is quite common in strict Mohammedans, who never take alcohol, and many of the Hindu patients had not indulged in it, while very few of them had drunk to excess. One-fifth of the cases were secondary to kala-azar, being partly of the special intralobular form described by the writer, but also commonly of the ordinary multilobular type or both varieties combined. There was no evidence that malaria ever produced a clinically evident cirrhosis, which is in accordance with Osler's experience in Baltimore. Hanot's biliary cirrhosis is rare in Calcutta, but a somewhat similar and very fatal form, with great enlargement of the liver, is met with in infants. Dysenteric lesions were found in 48 per cent. of ordinary cirrhosis and in 42.6 per cent of kala-azar cases. In over three-fourths of each form the lesions were old and probably antecedent to the cirrhosis, thus affording strong evidence of a causal relationship. The dysentery was usually of the amebic type. Gastric or duodenal ulcers were also met with several times. Chronic inflammatory changes in the gastrointestinal tract due to toxic absorption or bacterial infection through ulcers in the gastrointestinal canal are, therefore, the main cause of hobnail liver, and the frequency of chronic dysentery accounts for the great excess of cirrhosis in Calcutta.

Leucocytosis is common in ordinary cirrhosis of the liver, a high degree being of immediate very bad prognostic significance. On the other

hand, a marked leucopenia is diagnostic of the disease being secondary to kala-azar. Leonard Rogers (*Lancet*, Aug. 10, 1912).

We must, however, recognize clearly that alcohol is far from being the only agent which brings about exhaustion or lowered vitality of the liver-cells. There is, for example, one group of cases of cirrhosis of the portal or Laennec type in which the researches of recent years indicate forcibly that hematogenous toxins are implicated. We refer to the cases of splenomegaly with subsequent development of hepatic cirrhosis. The condition is often familial, and is apt to manifest itself in youth. Banti (*Trans. First Internat. Pathol. Congress, Turin, 1911*) more particularly has called attention to the fact that in an important group of these cases, if not in all, we deal with a hemolytic splenomegaly—a condition in which there is an inherent overactivity of the cells of the splenic sinuses, whereby these cells take up not merely dead and dying erythrocytes, but the functional red corpuscles. This overactivity explains, according to him, both the splenic hypertrophy and the anemia, and his view is substantiated by the fact that extirpation of the spleen in these cases is followed time after time by disappearance of the anemia and return to robust health. The development of cirrhosis in these cases must be associated with the overwork and irritation of the liver-cells in dealing with the products of the disintegrated red corpuscles conveyed by the portal blood from the spleen.

There has been a tendency exhibited by many pathologists to make minute and complicated classi-

fications based on pattern designs. But, if it is borne in mind that the liver cells are all alike, sharing equally in function, and that the natural reaction of the liver to chronic irritants, without regard to kind, is the development of connective tissue, the basic fact will be established, without being lost in a mass of morphologic detail. On the contrary, the response of the liver to acute destructive irritants, whether bacterial, toxic, or chemical, is in the nature of an acute fatty degeneration. W. J. Mayo (*Trans. Amer. Surg. Assoc., June, 1918*).

Yet another group of cases, as suggested by Budd, appears to be associated not with alcohol as the gastric and hepatic irritant, but with highly seasoned foods. We are alluding to the cirrhosis, already referred to, encountered among the natives of India, who never partake of alcohol, but consume much highly spiced food.

The writer, in 12,761 autopsies analyzed, found 198 cases of hepatic cirrhosis. Out of the latter number, 26.19 per cent. were due to infections; 13.42 per cent. to cancer; 2.4 per cent. to kidney disease. Blumenau (*Arch. f. Verd.-Krankh., xxvii, i, 1920*).

In 1200 autopsies analyzed by the writer, 8.5 per cent. of the adults showed hepatic cirrhosis, 80 per cent. of which were of the nodular type. Syphilis, with deforming bands of scar tissue, was responsible for 3 cases. Owen (*Amer. Jour. Syph., Jan., 1921*).

Let me emphasize that for clinical purposes we may reduce these to three main forms: (1) Portal, or Laennec's, cirrhosis; (2) infective biliary, or Hanot's, cirrhosis; (3) obstructive biliary cirrhosis. So also, while, as in the congenital form of the disease, syphilis may induce so widespread a

fibrosis that this comes under the definition of a true cirrhosis, the sharply defined and localized fibrous overgrowths of acquired syphilis cannot be regarded as cirrhosis proper. In other words, while syphilitic cirrhosis does exist, it does not come under the common types of this condition. Here, save in the matter of terminology, I find myself wholly in agreement with Rolleston, whose "Diseases of the Liver," published in 1905, takes the position held for long years by Murchison's great work, and may with confidence be said to be the most authoritative presentation of the subject of our generation. Rolleston retains the name "hypertrophic biliary" for what, following the French, I term Hanot's cirrhosis. Such painful confusion has followed the use of these terms, atrophic and hypertrophic, that I would banish them altogether.

After a study of a large number of cases of cirrhosis of the liver, the writer divides this lesion into five groups. The first group consists of the toxic cirrhosis, which includes the cirrhoses following central necrosis of the liver and is best exemplified by the acute yellow atrophy. A study of these cases seems to show that when all the liver-cells of a lobule were destroyed the bile-ducts grow out a certain distance toward the hepatic vein, but they do not produce liver-cells. Liver-cells, on the other hand, originate only from liver-cells and never from bile-duct epithelium. The production of fibroblasts (of new connective tissue) depends upon something more than the mere destruction of liver-cells. The other four types of lesions terminating in cirrhosis show that fibroblasts multiply only when fibroblasts themselves have been injured or disturbed and thus lead to increase of the connective tissue. The second group consists of the infectious cirrhoses. This is com-

paratively a rare lesion. Infection travels along the portal spaces, causing an inflammatory reaction in this region, with formation of new connective tissue. In the third group, or the pigment cirrhoses, there is a direct lesion of the fibroblasts which comes with the deposition of pigment. Alcoholic cirrhosis, which forms the fourth group, is characterized by a peculiar hyaline degeneration of the cytoplasm of the liver-cells preceding necrosis. In this same type the contraction of the connective tissue frequently compresses groups of liver-cells so that they resemble bile-ducts, but in these compressed liver-cells it is often possible to demonstrate large fat vacuoles or hyaline material due to degeneration in the cytoplasm, neither of which occurs in the true bile-duct epithelium. In syphilitic infection of the liver, which represents the last group, the primary injury is due to the fibroblasts, in consequence of which they often proliferate in excess. Contraction later of the collagen fibers produced by them results in compression and atrophy of the included liver-cells. This direct injury to the fibroblasts by the *Spirocheta pallida* seems to be a general one and characterizes the specific action of this organism. Mallory (Johns Hopkins Hosp. Bull., vol. xxii, p. 69, 1911).

## PORTAL CIRRHOSIS.

**VARIETIES OF PORTAL CIRRHOSIS.**—Thus far I have treated of portal cirrhosis in general, but it must be recognized that there are several varieties and stages in which the condition may manifest itself. The unfortunate employment of the term "atrophic" has led to not a little confusion and failure to recognize that these several varieties are but manifestations of one and the same process.

It may, in the first place, be questioned whether the disease always presents the same slow rate of develop-

ment. Apparently this is not the case; we may have either acute or chronic liver changes, which, strictly speaking, belong to the same group. The London school of pathologists is inclined to recognize the red atrophic liver, characterized by the presence of large islands of yellow, fatty degenerated parenchyma surrounded by greatly reddened congested tissue, which, under the microscope, shows abundant signs of a subacute productive inflammatory condition, with leucocytic infiltration and the development of new connective tissue. But the amount of this new connective tissue is hardly sufficient to justify us in regarding this as a condition of cirrhosis proper.

The cases brought forward by Cayley and Carrington and others all appear to be of this nature. There is a history of excessive indulgence in alcoholism, of preliminary slight gastric disturbance with signs of epigastric oppression, contraction of the liver, and development of ascites accompanied by more or less jaundice. The gross appearance of the liver is not greatly unlike that of acute yellow atrophy; but death takes place not in a few days or weeks, but in two or three months after the first symptoms are complained of.

On the whole, therefore, I am inclined to classify this red atrophy as the acute representative of the disease which, in chronic form, is portal cirrhosis, and, doing this, to recognize a series of grades of degeneration of the hepatic parenchyma, beginning with the very acute and rapidly fatal acute yellow atrophy, and passing through the less acute red atrophy to portal cirrhosis. I would, that is, class myself with those who believe that parenchymatous degeneration is an essential portion of the cirrhosis process.

As will be readily understood, cases of cirrhosis are, in the nature of things, chronic; acute red atrophy, therefore, is not to be included among the cirrhotoses proper.

Thus, to classify the different varieties of portal cirrhosis we recognize:—

1. **The Enlarged Fatty Cirrhotic Liver.**—The organ is markedly enlarged, shows but slight nodulation, and microscopically presents a not-far-advanced condition of cirrhosis. In a large number of cases it is unaccompanied by ascites, although the spleen may be enlarged; it occurs essentially in alcoholics and may not be recognized until after death from some intercurrent disease.

2. **The Atrophic Hobnailed Liver.**—The characteristic form of the disease. The organ greatly reduced in size, with surface studded with nodules of varying size, generally small; very dense and leathery; generally accompanied by marked ascites and other evidences of portal obstruction, and enlarged spleen. On section, of yellowish-red color, showing well-developed, glistening bands of fibrous tissue separating off small islands of the parenchyma.

3. **Portal Cirrhosis with Secondary Parenchymatous Hypertrophy.**—The hypertrophic, alcoholic cirrhosis of French writers. The organ larger than, but similar in character to, the preceding form. There is a considerable amount of confusion about this form, owing to the use of the term "hypertrophic." It has often been confused with the biliary cirrhosis of the type studied more especially by Hanot, while, again, others confound with this the intermediate stage between the enlarged fatty cirrhotic liver and the small atrophic organ, and again cases of mixed biliary and portal cirrhosis.

The true hypertrophic cirrhosis of this type is the "large hobnailed" liver; the organ presents a nodular surface, some of the nodules being of a relatively large size. The weight is normal or above the normal, and the enlarged size appears to be due, in the main, to compensatory overgrowth of some of the isolated lobular masses and to a partial recovery of the organ from the effect of the cirrhosis.

**4. Portal Cirrhosis with Adenomatous or Adenocarcinomatous Overgrowth.**—The distinction between the last condition of cirrhosis with parenchymatous hypertrophy and cirrhosis with generalized adenomatous condition is very subtle, and, as shown in connection with Fussell and Kelly's first case (*Trans. Assoc. Amer. Physic.*, vol. x, p. 116, 1895), good authorities may differ as to whether a liver presents the one or the other condition. On the other hand, there may be such extensive overgrowth and multiple formation of large neoplastic masses that there can be no doubt as to the cancerous nature.

In the majority of these cases the cirrhosis seems to be of the mixed kind, being multilobular and at the same time presenting abundant formation of new bile-canaliculi: an indication that possibly the following form is not truly a mixed portal and biliary cirrhosis, but a portal cirrhosis with parenchymatous hypertrophy, one of the indications of the hypertrophy being a proliferation of the bile-canaliculi.

**5. Mixed Cirrhosis.**—A very large number of cases must anatomically be classed under the heading of mixed cirrhosis, though the gross appearance of the organ and the clinical history bring them definitely into the category of portal cirrhosis. The condition is, in the main, multilobular, but there is

abundant formation of new bile-canaliculi. The organ, again, in general, approximates to the normal size, and there is not the extreme atrophy seen in the uncomplicated cirrhosis.

**6. Portal Cirrhosis with Pigmentation.**—In the majority of cases of portal cirrhosis examined by Dr. Maude Abbott (*Jour. of Pathol.*, vol. vii, 1901, p. 55) there was found a distinct increase in the amount of iron in the liver, as demonstrated by Perl's test (acid and potassium ferrocyanide); in some the amount is so great that the organ assumes a brick-red color. French observers (Troisier, 1871; Hanot and Chauffard, Letulle, Auscher and Lopicque, Gilbert, and several others) noted this increase particularly in association with diabetes, and, as coincidentally there is pigmentation of the skin, they treat the cirrhosis as of less importance and refer to the condition as "diabète bronzé." German authorities, following von Recklinghausen (Hintze, Lubarsch, Auschütz, etc.), lay stress upon the diffuse deposits of iron-containing pigment not only in the liver, but in non-striated muscle, more especially of the intestines, in the lymphatic glands, pancreas, spleen, salivary glands, and skin, and regard the cirrhosis, both of the liver and the pancreas, as a complicating condition of this state of "hemochromatosis." In the first edition of this work I referred briefly to a case encountered by me; that note was, I believe, the first recognition of the condition upon this continent. Since then the same case has been exhaustively studied and described by Dr. M. E. Abbott, although prior to her publication Opie (*Jour. Exp. Med.*, vol. iv, 1899, p. 279) brought out a very full description of a case encountered at Baltimore. Osler and Condon have

described other cases. In England Saundby, Galloway, G. Parker, and Rolleston have recorded cases. Only in France does the association with diabetes appear to be the more frequent event. Even there it is rare. Fitcher, in 1907 (Amer. Jour. Med. Sciences, vol. cxxxiii, p. 93), could collect only 35 undoubted cases. When encountered the condition is striking. The pigmentation of the skin may suggest Addison's disease, but often is of a sallower, more earthy type; in one case it was so advanced that the patient was known through the hospital as "blue Mary." The liver in general is of the enlarged cirrhotic type, exhibiting multilobular cirrhosis. The spleen also is enlarged. Fibrosis of the pancreas and diabetes, as above stated, may or may not be present. Opie would regard this combination of cirrhosis with hemochromatosis as a condition *sui generis*. Abbott and the writer brought forward evidence indicating that both the hemochromatosis and the cirrhotic changes are due to chronic intestinal infection—to the entry into the portal system of organisms possessing pronounced hemolytic properties, causing destruction of the red corpuscles and liberation of their hemoglobin. This view has gained not a little support of late years by the recognition of rare cases of acute bacterial cyanosis by Stokvis and other Dutch observers; by Gibson, of Edinburgh; Blackader, of Montreal, and others—cases that are of acute cyanosis and cutaneous pigmentation due to a bacillus coli bacteremia, the colon bacillus possessing definite hemolytic properties.

It is evident, therefore, that in a large proportion of cases of ordinary cirrhosis there is increased destruction of the red blood-corpuscles—whether

brought about by hemolytic bacterial agencies or by the hemolytic action of the spleen.

**SYMPTOMS.**—The condition of portal cirrhosis begins insidiously and may continue to an extreme condition without producing any symptoms which call attention to the existence of the process. Very frequently the earliest symptoms are associated with the alimentary tract; next in order are evidences of portal obstruction, and only when the condition is very well marked may there be disturbances referable to the hepatic function. Whether the gastric and intestinal disturbances are primary or secondary is a matter concerning which there has been debate. That they are not entirely due to the overfilling of the gastric and intestinal vessels in consequence of the portal obstruction is, I think, evident from the fact that they appear long before any signs of such obstruction show themselves, and if we ascribe alcoholic cirrhosis not so much to the alcohol itself as to the pathological condition of the stomach and intestines whereby either toxic substances are absorbed from the food, or there is developed a state of "subinfection" by increased passage of intestinal bacteria into the portal circulation, we must regard this as being the earliest disturbance in the course of the disease. That at a later period the abdominal congestion further militates against the proper performance of the gastric and intestinal functions there can be no doubt. It will be well, therefore, to subdivide the symptoms into:—

1. The disturbances occurring in connection with the alimentary tract.
2. Symptoms of vascular obstruction.
3. Symptoms referable to disordered function of the liver and to altered metabolism.



**Symptoms Referable to Gastric and Intestinal Disturbance.**—Of these the most noticeable are: at the very earliest stage slight dyspepsia, morning vomiting or nausea, and furred tongue; added to this there may be eructations and irregularity of the bowels. There is often an alternation of constipation and catarrhal diarrhea. During the former of these the stools often present remarkable modifications: some days they are normal; then they become very dry and are covered with a thick layer of mucus; at other times they are colorless, and, as Graves has pointed out, in the same stool one may find portions which are gray, clayey, and others of normal color. To these disturbances of the digestive system may be largely attributed the emaciation of the later stages of the disease. With these, as Bright was the first to note or as Rolleston emphasizes at autopsy, there is frequently found a noticeable shortening of both the small and the large intestines: the walls are thickened as from a chronic enteritis; the mesenteries also thickened.

Examination of the contents of the stomach showed typical cases of gastrosuccorhea, one of continuous hypersecretion, the other of intermittent or periodic hypersecretion. This gastric symptomatology represented, at the time the cases first came under observation, the prominent and only definite symptoms present. Hewes (Boston Med. and Surg. Jour., Aug. 16, 1906).

The writer has tested the stomach content for occult blood in every case examined in recent years. Among the discoveries made is the constant finding of occult blood in the stomach content and stool in 2 cases of what proved to be later cirrhosis of the liver. The discovery of occult blood may thus prove a sign of this affection in its earliest, still symptomless

stage. Lifschütz (Archiv f. Verdauungskrankheiten, Bd. xv, Nu. 1, 1909).

The writer terms "gastrohydrorhea" the flow of a watery fluid from the stomach containing neither hydrochloric acid nor rennet or pepsin ferments. One to 1½ quarts (liters) a day occurred in a patient suffering from cirrhosis of the liver accompanied by a pyloric stenosis. No ascites had developed. At autopsy a typical cirrhotic liver and a pyloric tumor (cancerous) were found. Max Einhorn (Trans. Assoc. Amer. Phys.; Med. Rec., Aug. 12, 1916).

**Symptoms Referable to Disturbances of the Circulation.**—So long as there is a well-established collateral circulation, for so long will there be no symptoms referable to obstruction. It is only when this collateral circulation becomes inadequate to carry the portal blood to the heart that ascites and other obstructive disturbances supervene. Thus, not infrequently we meet with extensive portal cirrhosis without a sign of ascites. Very frequently, however, the nature of this collateral circulation is the direct cause of death; more especially is this the case with the plexus of submucous veins at the lower end of the esophagus, which plays a prominent part in this collateral circulation. These veins, being practically unsupported toward the free surface of the esophagus, become varicose and relatively enormous; the patient may appear in very fair health and the liver be performing its functions satisfactorily with but a thirty-second of an inch or less intervening between life and death, for it is these varicose subesophageal veins which are especially liable to rupture and to produce so extreme a hemorrhage that death follows in the course of a few hours.



Abdominal Varices in Cirrhosis of Liver. (*Schapiro.*)

St. Petersburg med. Wochenschrift.



Fatal gastrointestinal hemorrhage is an infrequent, but not rare complication of cirrhosis of the liver. The cirrhosis is generally atrophic, although it may be hypertrophic. In one-third of the cases the hemorrhage is fatal; in the others they continue at intervals for varying periods of time—even eleven years. In one-third of the cases, diagnosis can be made at or before the time of the first hemorrhage; in the others, only after months or years. Esophageal varices are present in 80 per cent. of the cases, and in many of them are seen macroscopic ruptures. Fatal hemorrhages in cases showing no esophageal varices are probably due to the simultaneous rupture of capillaries of the gastrointestinal mucous membrane. In only 6 per cent. of the cases showing esophageal varices was the cirrhosis typical. R. B. Preble (*Amer. Jour. Med. Sci.*, March, 1900).

Hemorrhages of varying grade are common even in advanced stages of cirrhosis of the liver. They occur usually in from 12 to 15 per cent. of cases, and Hardicti observed them in 30 of 52 cases. Of special interest, however, are patients in whom a profuse hemorrhage is the first symptom of the disease. The tendency of such hemorrhages to recur prompted Maixner to draw a special clinical picture. The cause of the hemorrhage is the portal obstruction, leading to intense congestion in its radicles and the formation of large varices in the areas where collateral circulation is established. It has been frequently shown at autopsy that the bleeding has come from the rupture of such varices, and the enlarged veins in the lower portion of the esophagus are a favorite point of origin for the hemorrhage. In other instances the hemorrhage seems to be a capillary oozing or to come from erosions. A special feature of Maixner's cases and of those reported by the writer is the very large size of the spleen, a size extremely unusual in cirrhosis of the liver. One is immediately struck with the clinical

resemblance to Banti's disease or splenic anemia. Von Aldor (*Berl. klin. Woch.*, Bd. xlii, S. 1115, 1905).

The best account of this collateral circulation is given by Osler and we here recapitulate it:—

"The compensatory circulation is usually readily demonstrated. It is carried out by the following set of vessels: 1. The accessory portal system of Sappey, of which important branches pass in the round and suspensory ligaments and unite with the epigastric and mammary systems. These vessels are numerous and small. Occasionally a large single vein, which may attain the size of the little finger, passes from the hilus of the liver in the round ligament and joins the epigastric veins at the navel. Although this has the position of the umbilical vein, it is usually, as Sappey showed, a paraumbilical vein, that is, an enlarged vein by the side of the obliterated umbilical vessel. There may be produced about the navel a large bunch of varices: the so-called *caput Medusæ*. (A case of abdominal varices is shown on the annexed plate.) Other branches of this system occur in the gastroepiploic omentum, about the gall-bladder, and, most important of all, in the suspensory ligament. These latter form large branches, which anastomose freely with the diaphragmatic veins, and so unite with the vena azygos. 2. By the anastomosis between the esophageal and gastric veins. The veins at the lower end of the esophagus may be enormously enlarged, producing varices which project on the mucous membrane. 3. The communications between the hemorrhoidal and the inferior mesenteric veins. The freedom of communication in this direction is very variable, and in some instances the hemor-

rhoidal veins are not much enlarged. 4. The veins of Retzius, which unite the radicles of the portal branches in the intestines and mesentery with the inferior vena cava and its branches. To this system belong the whole group of retroperitoneal veins, which are, in most instances, enormously enlarged, particularly about the kidneys, and which serve to carry off a considerable proportion of the blood."

The writer has frequently observed that the subcutaneous veins of the forearm in cases of atrophic hepatic cirrhosis pulsate vigorously. The pulsation is synchronous with the cardiac action. Inspiration produces marked collapse of the vein, and there is a negative venous pulse. This applies also to the jugular veins. The phenomenon may be temporary or may persist during the whole course of the disease. It is most marked in the cutaneous veins on the radial side of the arm. If it temporarily disappears it can be made to return by warming the arm or allowing it to hang by the side until the veins become distended. Aspiration of ~~ascites~~ ~~fluid~~ has practically no influence on it. The variety of cirrhosis is immaterial, and a venous pulse may occur in alcoholic, syphilitic, or cardiac cirrhosis in the atrophic stage. It is, therefore, probably due to a modification of the venous circulation by pressure on the portal vein. Hitschmann (Zentralbl. f. inn. Med., Jan. 16, 1904).

But in addition to the disturbance in the portal circulation, there appears to be also a frequent accompanying disturbance in the general circulation. It may here be more correct—inasmuch as this disturbance seems to be largely associated with alterations in the blood brought about by the hepatic disturbance—to refer to this under a later heading.

Abdominal plethora is not the only cause of hemorrhage from the di-

gestive tract in cirrhosis. The hemorrhages that occur at a distance from the region of the portal vein and which are frequent in cirrhosis cannot be accounted for by abdominal plethora. Extra-abdominal hemorrhages in patients suffering from cirrhosis are related to pre-existing arterial lesions that may result in the production of nevi in the skin, in the mucous membrane of the mouth, of the pharynx or of the esophagus. The gastrorrhagias of the cirrhotics have their origin, also, in pre-existing arterial lesions. Epistaxis from an arterial lesion has intimate relations with cirrhosis. Ch. Bouchard (Revue de méd., Oct. 10, 1902).

**Ascites.**—The ascites of portal cirrhosis develops gradually, and in this way is to be distinguished from that following thrombosis of the portal vein. While it is a very prominent and characteristic symptom of the condition, it must be remembered that it is far from being constantly present. Indeed, I may go farther and point out that much of the failure of clinicians to recognize portal cirrhosis is due to the erroneous belief that ascites almost constantly develops. *It does not by any means*; only in advanced atrophic cases is it the rule.

The writer found ascites in 172 out of 250 cadavers with cirrhosis of the liver. These findings indicate that the same toxic cause inducing the cirrhosis is also responsible for the ascites. The frequency of coincident intestinal tuberculosis was also striking. The absence of ascites in 2 instances shows that the effusion is not responsible for the predisposition to the tuberculous affection. Cirrhosis of the liver may also result directly from tuberculous infection. Although the prevalence of cirrhosis of the liver in hard drinkers and the predisposing influence of alcohol are not to be denied, yet the decisive rôle in the production of the affection does not belong to them, but to bacteria

and their toxins. The writer noted cholelithiasis in 8.6 per cent. of 209 men, and in 17 per cent. of the 41 women in his material. Klopstock (Virchow's Archiv, Bd. clxxxvii, Nu. 1, 1907).

The older writers speak of it as being present in about 80 per cent. of the cases; more recent careful observers give a lower proportion, thus: Rolleston and Fenton found from the post-mortem records at St. George's Hospital in London, that of 114 cases only 36, or a little over 30 per cent., showed ascites. In a fuller, more recent study of 166 consecutive post mortems upon cirrhosis at this same hospital Rolleston found that 86, or just over half, presented no ascites. Kelynack, in 121 examples of common hepatic cirrhosis, as he terms it, coming to the post-mortem room at the Manchester Royal Infirmary, found ascites in 56 per cent.

[Rolleston speaks of these as "latent cirrhosis." Clinically the expression is accurate; unless there be ascites although the liver be contracted above the margin of the ribs, the clinician does not diagnose portal cirrhosis. There are, however, distinct dangers in this use of the term, first, that it leads the physician to regard cirrhosis as a negligible condition so long as ascites is absent, and thus to overlook the significance of the dyspepsia and other gastrointestinal disturbances which may be present, as again the significance of the tuberculous and other complications which so frequently show themselves in these "latent" cases, and, second, because where, as is often the case, he deals with the large, early liver of portal cirrhosis, and diagnoses its hobnailed condition, he becomes apt—in the absence of ascites—to regard this as some other type of cirrhosis, to speak of hypertrophic cirrhosis, and regard the condition as a separate entity. It is better to hold on to the conception that cirrhosis is a progressive disorder in which ascites is a possible late event. Saying this, I am far from wishing to in-

dicate that cases do not occur in which the inflammatory process which has induced the cirrhosis does not become arrested. The large, hobnailed liver of secondary parenchymatous hypertrophy, already described, belongs to this category. I would prefer to speak of this as "arrested" rather than latent. J. GEORGE ADAMI.]

The fluid in these cases is clear, but may be slightly bile-stained; after repeated tapping it assumes more the character of an inflammatory exudate. According to some French observers, it begins as a subacute peritonitis, and in favor of this view, or more accurately of the view that combined with an ascites of mechanical origin there is a low inflammatory disturbance, I may note that from the fluid of first tapplings made with all aseptic precautions I have repeatedly (although not in every case) gained cultures of attenuated members of the *B. coli* group. These are not abundant; relatively large amounts of the fluid must be taken in order to gain results. The fluid is alkaline, with a specific gravity varying between 1010 and 1015, though, if there has been any peritonitis, this specific gravity and the percentage of proteid are increased and the fluid may show spontaneous coagulation. Hale White, in his article on "Perihepatitis" (Allbutt's "System of Medicine"), holds that ascites proper is a late event in cirrhosis, for which more than one tapping is rarely required, and regards those cases in which multiple tapplings are necessary as being complicated with peritonitis; indeed, he goes so far as to hold that, where ascites is directly due to cirrhosis and paracentesis is necessitated, the patient rarely lives long enough after the first tapping for the second to be necessary. Of 10 cases which were recorded during life as

having cirrhosis, but were tapped oftener than once, of 4 at post-mortem examination, 3 were found to be cases of chronic peritonitis and perihepatitis and 1 of colloid disease of the peritoneum; the remaining 6 had more or less chronic peritonitis associated with the cirrhosis which was present. In fact, he would employ this as of diagnostic value as between uncomplicated cirrhosis and peritonitis or perihepatitis with or without cirrhosis.

[But this view has not gained by any means universal acceptance. Thus, Casati has recorded a case in which tapping was performed 111 times, and MacDonald 2 cases which were tapped 31 and 60 times, respectively, before the ascites disappeared. In opposition it may be said that these repeated tapings must have induced peritonitis, even if this were not present from the first. J. GEORGE ADAMI.]

As to the cause of the ascites opinion is being more and more strongly expressed that portal narrowing alone, through contraction of the fibrous tissue, is not the cause. Clearly when the liver becomes greatly contracted the portal territory within the liver is diminished, and with the smaller field there must be some obstruction. What is striking, however, is the continued vascularity of the organ. As Kelly points out, there is evidence of the development of short circuiting of collateral circulation between branches of the portal and hepatic veins.

Herrick (*Journal of Experimental Medicine*, vol. ix, 1907, page 93) has called attention to a very possible cause of obstructed outflow of the portal blood, namely, to the increased arterial circulation and enlargement of the hepatic artery and its branches in portal cirrhosis. The increased arterial pressure so induced in the capillaries of the lobules and elsewhere common to

arteries and portal vein must, he urges, hinder the circulation in the latter.

**Edema** of the feet is not infrequently secondary to ascites, and is, in the main, due to a pressure of the distended abdominal contents upon the veins coming from the lower extremities. According to Osler, edema of the feet may precede the development of the ascites, in which case it is to be ascribed to the malnutrition of the patient and the impoverished condition of the blood. The dropsy rarely becomes general.

Case of angioneurotic edema associated with cirrhosis of the liver in a male patient aged 40 years. There was swelling of both ankles, and pain which prevented him from walking. The patient had suffered from this condition for three years. On examination there was found edema of both feet and ankles, which were tender on pressure. All the veins of the lower extremities, together with the superficial abdominal veins, were varicose and distended, and an enlarged vein was present in each axilla. Slight enlargement of the liver was evident, and there was reason to believe that some degree of cirrhosis of that organ was present. The heart and lungs were normal. There was nothing notable in the family history or previous illnesses of the patient except that about three years ago he sustained a fracture of the tibia, from which time he dates his edema and varicose veins. The urine was normal.

Under rest, total abstinence, and Scott's dressing applied to the ankles he recovered in three weeks and was able to walk without pain. About a month later, while in bed, his upper lip suddenly swelled up. On the next morning there was a tense swelling in the left side of his upper lip. The swelling subsided during the day, but next night his lower lip became similarly affected, and a swelling developed in the neck. Night after night a lump appeared in a new place.

Once the whole tongue was swollen up, so that he could not protrude it. On another occasion the scrotum became tense and edematous. S. G. Corner (*Lancet*, July 31, 1909).

The writer observed a case of central cirrhosis of the liver with vegetative endocarditis of gonorrheal origin in a young man 22 years of age, following an acute attack of acute specific urethritis. The clinical features of the case were fever with delirium, dyspnea, hemoptysis and icterus, and moderate generalized edema. The course of the disease was about 8 weeks. V. H. Bassett (*Med. Rec.*, Jan. 3, 1914).

In looking over the records of 60 cases of cirrhosis in adults, abuse of alcohol was found in 35 per cent., but in 39 alcohol could not possibly be incriminated. In 15 per cent. there was a history of chronic malaria. In 4 of the women no cause for the cirrhosis could be detected. In 5 per cent. of the total, syphilis may have contributed although 1 of the 12 in this group was a habitual drinker. Banti's cirrhosis seems to be anatomically identical with Laennec's cirrhosis; of the 7 cases of this kind, none had a history of abuse of alcohol. Consequently it is incorrect to call Laennec's cirrhosis alcoholic cirrhosis. L. Urrutia (*Siglo Medico*, Dec. 21, 1918).

**Enlargement of the Spleen.**—This is far more frequent than is ascites. Thierfelder found, out of 172 cases, only 39, or 22 to 23 per cent., in which this symptom was absent; indeed, it may be regarded as the most common of the symptoms associated with portal cirrhosis. The enlargement is, in general, not so marked as in biliary cirrhosis (Hanot's); the organ averages between one and a half times to twice the normal weight. Oestreich is inclined to believe that this enlargement of the spleen is not entirely due to portal obstruction, in that it appears at so

early a stage of the condition before other marked signs of such obstruction are evident; indeed, it is suggested that the toxic causes which are at work to produce the hepatic lesion bring about enlargement of the spleen.

In cases of cardiac disease which have caused chronic passive congestion of the abdominal viscera the spleen is usually firmer than normal. The question, therefore, arises: Is there with this increase also an increase in the framework of the spleen? This question he answers as follows: In 38 cases of chronic passive congestion and cirrhosis of the liver, the spleen of 28 (73.6 per cent.) shows an increase in connective-tissue framework. Some of the 10 cases with no increase in connective tissue are equally as firm; consequently the firm consistence in these is due to vascular distention rather than to connective-tissue increase, and in all cases vascular distention probably plays an important part in producing the firm consistence. The connective-tissue increase is mainly a proliferation of the reticular tissue of the pulp with little or no change in the white fibrous and elastic tissue of the organ. Christian (*Jour. Amer. Med. Assoc.*, Nov. 25, 1905).

Weber, like Oestreich, is of the opinion that toxemia is the cause of the enlargement. The organ is enlarged from one-half to three times its normal size; in one case of portal cirrhosis which recently came under my notice, it weighed 720 grams. Describing a similar case of large splenic tumor, Banti compares it with the malarial spleen, and urges the probable infectious origin of such cases.

The changes observed in the spleen with cirrhosis of the liver should not be confounded with the changes and enlargement of the spleen from chronic congestion.

The etiological factor which provokes the lesions in the liver acts



on the spleen in much the same way. Changes are found in other organs, such as the transformation of the yellow bone-marrow into red marrow, which has been cited as an argument in favor of the assumption that cirrhosis of the liver is primarily an affection of the blood. Egidi (Policlinico, Medical Section, Sept., 1909).

**Hemorrhoids.**—While hemorrhoids are frequent in cases of portal cirrhosis, the majority of recent writers are of the opinion that they are far from being as common as used to be taught.

**Pain and Tenderness.**—Pain over the region of the liver is often most noticeable in the early stages, and is often accompanied by a sense of epigastric fullness and tension, which may be present through the duration of the disease. As Ross pointed out and explained in his remarkable article in the tenth volume of *Brain*, besides these sensations referred directly to the diseased organ (or conditions of *splanchnic* pain), there may be other painful sensations which may be termed *somatic*, or referred pains. The liver is innervated from the seventh to the tenth dorsal, and, as a consequence, the pain affecting the organ may be referred to the cutaneous branches of these nerves by overflow of irritation in the cord, and, as a matter of fact, pain is frequently felt in the region of the angle of the right scapula. Another pain at times experienced is that at the tip of the right shoulder, more rarely of both shoulders. Where this is the case there is an indication of involvement of the upper surface of the organ, extending to the diaphragm, for such pain is brought about by the overflow of irritation at the point of entry of the phrenic nerve into the spinal cord, and so there is reference to pain along the branches of the lower cervical

nerves, the phrenic arising chiefly from the fourth cervical with a few filaments from the third.

**Symptoms Referable to Disturbed Function.**—**Wasting.**—This is a striking feature in advanced cases; the contrast between the distended, ascitic abdomen and the emaciated thorax, face, and extremities may be most marked.

**Jaundice.**—One of the most constant symptoms of portal cirrhosis is a slight icteroid tinge of the conjunctivæ accompanied by a bright, watery appearance of the eyes. The skin, in general, save where there is frank development of ascites, is pale rather than icteroid, but as the disease progresses the face gains a sallow, ashy tinge. In the very rare extreme cases of pigmentary cirrhosis the skin may assume a slaty blue, or in some cases, as in diabetic cirrhosis, a bronzed appearance similar to that seen in Addison's disease.

Jaundice, however, may show itself in any period of the disease; it is characterized by not presenting that continuous and progressive severity observable in cases of true biliary cirrhosis. According to Fagge, at Guy's Hospital, out of 130 cases, only 35 showed this symptom, or just under 27 per cent.; Rolleston, combining the statistics of 293 cases of other ascites, found jaundice recorded in 107, or 36.5 per cent.

**Urine.**—In the earlier stages there may be little or no change, but, as the condition progresses, the quantity diminishes in amount, the color becomes dark, and, as Hayem and von Jaksch have pointed out, the greatly increased amount of urobilin is an indication of considerable value where the diagnosis is doubtful. Save where there is a frank condition of jaundice, bile-pigments are absent. The urea is often found diminished, as also are the chlo-

rides when ascites is present; the urates, on the other hand, markedly increased. Albumin is, at times, present, with casts, apart from those casts which may be associated with jaundice. Kely-nack found renal cirrhosis present in a little over 18½ per cent. of his cases.

The presence of a strong perchloride of iron reaction in the urine of several patients suffering from hepatic cirrhosis noted. The color obtained was sometimes similar to that seen in the presence of diacetic acid in diabetes mellitus, and sometimes to that obtained when salicylic acid has been taken. The appearance of the reaction sometimes coincided with very threatening general symptoms. Weber (Brit. Med. Jour., Jan. 2, 1904).

The writer reviews the literature of the levulosuria test in hepatic cirrhosis and gives details of his own experiments made by administering 100 Gm. (3½ ounces) of levulose dissolved in 500 c.c. (1 pint) of tea or water on a fasting stomach after the morning evacuation of the bladder. The urine was collected each hour, for four successive hours, in 4 separate bottles, after which breakfast was taken. Each specimen, including that passed before the beginning of the test, was examined separately by the Fehling, Nylander, Seliwanoff, and fermentation tests, and the combined urine after the administration of the levulose by the above tests and, in addition, by Rosin's method and by the polariscope. As the number of cases increased, the spectroscopic examination was omitted. The results are tabulated in the case of 32 patients suffering from cirrhosis or congestion of the liver in all but two or three cases. He sums up his results as follows: "1. Alimentary levulosuria is almost a constant phenomenon in cirrhosis of the liver. 2. The early or late appearance of levulose may be regarded as a sign of severe or mild hepatic disease. 3. Alimentary levulosuria is a useful aid

in diagnosing between cirrhosis, on the one hand, and chronic passive congestion, on the other. 4. A study of the hepatic function with glucose and with saccharose in addition to levulose is to be desired, inasmuch as there may be an individual intolerance to carbohydrates. 5. While not indicative of any specific organic lesion of the liver, alimentary levulosuria is most frequently observed in cirrhosis." E. H. Goodman (Jour. Amer. Med. Assoc., Dec. 18, 1909).

**Blood.**—There is very little that is characteristic about the condition of the blood in portal cirrhosis. There is no marked increase in leucocytes, no extensive diminution either of the hemoglobin or of the number of red blood-corpuscles, but the tendency toward epistaxis and the development of petechiæ in connection with the general, as opposed to the portal, circulation would seem to indicate that either the blood is of such a poor quality or contains such abnormal and toxic substances as to lead to degeneration of the capillary walls, and, as already pointed out, the occasional occurrence of edema preceding ascites is another indication of this toxic or impoverished condition of this fluid.

Two cases of hepatic cirrhosis without hemorrhage terminating in pernicious anemia. That such a change should occur in the blood is easily conceivable, when it is remembered that both hepatic cirrhosis and progressive pernicious anemia are probably due to infection. In any case, secondary and primary, or pernicious, anemia are but relative terms. Many of the cases formerly classed as primary latterly have been found to be secondary, the cause having been demonstrated. The differences in the blood-findings are, moreover, largely those of degree. Hemolysis and hematogenesis are present in both. J. E. Talley (Jour. Amer. Med. Assoc., Oct. 3, 1908).

The writers report 2 cases with marked hemolysis peculiar in that the liver showed atrophic instead of hypertrophic cirrhosis. They hold that the group of pigmented cirrhoses shows no essential difference from non-hepatic conditions with iron pigmentation of organs, but is the result of an hemolysis, similar to that of pernicious anemia. The recent finding of diminished resistance of the red corpuscles in "pigmentary cirrhoses" supports this view. Where the hemolysis is very intense, both iron and bile pigments are set free, and the resulting condition, sometimes met with in hepatic cirrhosis, is a hemolytic jaundice. Chali  and Nove-Josserand (*Revue de M d.*, May, 1913).

A further indication of the altered or thinned condition of the blood is the not-infrequent existence of a venous hum in the epigastric region noted by several recent observers and of a splenic souff le first noted by Bouchard.

Case of atrophic cirrhosis of the liver in a man of 49 years. The murmur, heard all over the sternum and hepatic area, was continuous, although consisting of two phases of intensity and duration, comparable to the passage of a strong wind through a fissure. Generally speaking, its greatest intensity corresponded with cardiac diastole; and it became more distinct as the ensiform appendix was approached, though not audible directly over that point. Up to the fourth intercostal space the murmur was heard solely over the sternum; but at that point it could be heard about 2 cm. to the left; and to the right, starting at the insertion of the fourth cartilage, it could be followed to the midaxillary line, thence to the costal arch, and at the mammary line its inferior limit descended to the eighth cartilage. V. Gambarati (*Riforma Medica*, Feb. 11, 1903).

Venous murmurs audible over and in the neighborhood of the spleen are relatively common in cirrhosis of the

liver, occurring in one-fifth to one-sixth of all the cases; murmurs audible elsewhere, as in the epigastrium, near the xiphoid, above the umbilicus, etc., are very uncommon and are still unexplained. In a marked case of hepatic cirrhosis, the veins about the umbilicus were somewhat dilated, those of the rest of the abdomen very markedly. The xiphoid, mammary, and inferior epigastric veins were markedly dilated and connected by a number of branches. Several centimeters to the left of the umbilicus the hand could feel an intense thrill, most marked over the left inferior epigastric vein; it was easily heard over the entire abdomen, but varied in intensity and character in different places. Compression of the left epigastric vein below the point of greatest intensity caused a disappearance of the murmur; below this point the vein was narrower than farther up. The murmur was evidently caused by the blood flowing suddenly from the relatively narrow inferior epigastric vein into the more dilated superior epigastric vein; the junction of the deep and superficial inferior epigastric was immediately below this point, increasing the pressure, and the blood-pressure was still farther increased by the stasis in the portal vein. In his second patient a venous murmur was audible but not palpable immediately below the ensiform cartilage; it was transmitted upward along the sternum. These murmurs, therefore, are due to the blood flowing under considerable pressure from a relatively narrow vein into a larger one, in which the pressure is considerably lower. Catti (*Zeitsch. f. klin. Med.*, lld. lxi, S. 269, 1907).

A venous hum, accompanied sometimes by a well-marked thrill, was detected by the writer in the epigastrium in some instances of hepatic cirrhosis. The thrill was appreciable: (a) directly over the extensive cutaneous varicosities, or (b) in instances where there is little or no external evidence of venous engorgement. In

most of the cases in which an epigastric venous hum has been heard in cirrhosis, in the absence of cutaneous varicosities, the sound has been audible best about the umbilicus and along the median line in the epigastrium—in other words, along the course of the round ligament. In a few of these instances it has been found that the incompletely closed umbilical vein has become greatly dilated as a result of increased portal pressure. In others, a large dilated vein has been found in the round ligament running alongside of the obliterated umbilical vessel—doubtless a dilatation of a small paraumbilical vein. These murmurs should be distinguished from the slight venous hum sometimes heard in the anemic just above and to the right of the umbilicus, over the inferior vena cava—murmurs which may be brought out by pressure in thin individuals. They are said to disappear in some cases with pressure on one or another femoral vein (Friedreich). W. S. Thayer (*Amer. Jour. Med. Sci.*, March, 1911).

Case of hepatic cirrhosis in which, over the ensiform cartilage, could be heard a very loud roaring murmur, localized to an area scarcely exceeding the space covered by the head of the stethoscope. It was continuous, but it had remissions in its loudness, there being a distinct inspiratory accentuation and a corresponding expiratory lessening. The murmur could be readily made to disappear by slight pressure of the stethoscope. The liver dullness was apparently about normal, although a slight quantity of fluid and gaseous distention of the abdomen interfered with accurate determination of the lower border of liver dullness. There was some edema of the ankles. The man rather suddenly became delirious and very ill, and on May 12, 1911, died of pulmonary edema. The autopsy revealed the following: Underlying the ensiform cartilage and extending to the articulation with the sternum there is found a venous sinus

about 7 mm. in diameter. Anteriorly there could be seen through an opening in the ensiform the anterior wall of this sinus. Proceeding from this opening were several small, superficial veins, probably in communication with the sinus. From this sinus there was a vein communicating with the vein in the suspensory ligament of the liver; this latter was somewhat dilated. Apparently there was no communication between the portal vein or inferior vena cava.

The entire lesion was contained within the mass of adhesions, between the anterior portion of the liver near its edge and the overlying ensiform and lower part of the sternum. The area occupied by the mass was about 4 by 2½ cm. J. N. Henry (*Amer. Jour. Med. Sci.*, Jan., 1912).

**Other Symptoms Referable to Disturbed Hepatic Function.**—Very characteristic toward the latter stage are certain nervous symptoms, which also are, in general, attributed to a toxic condition of the blood. These are, by some, classed as manifestations of cholemia, although, as they may be present when there is no evidence of the passage of bile into the blood, this use of the term is scarcely exact. I refer to the drowsiness of many patients and the more marked nervous conditions of coma and delirium. Where death is not due to hemorrhage or intercurrent disease, such as tuberculosis, it is these nervous disturbances which are the prominent feature in the fatal event. These nervous symptoms may be mistaken for the onset of uremia. There may be marked excitation, or, on the other hand, a progressive and deepening stupor passing into complete coma. As indicating hepatic incompetence and the passage into the blood of substances absorbed from the alimentary tract and unacted upon by the liver it is deserving of note that these same

symptoms have been observed after the Talma-Morison operation, whereby the portal blood is diverted through the abdominal walls.

Beginning cirrhosis of the liver may be strongly suspected if with irritability of temper, mental depression, insomnia, mental slowness, various nervous symptoms, the result of the toxemia, there is general decline of health; icteroid discoloration of the skin; feeling of weight or vague discomfort in the hypochondrium; loss of or capricious appetite; irregularity of the bowels; a broad, flabby, coated tongue; a foul breath; loss of weight; a muddy, leaden complexion, with a permanent dilatation of the cutaneous capillaries; a true telangiectasia in various parts of the body, especially in the face. Hubert Richardson (*Med. Record*, Oct. 8, 1904).

Case of Klippel's syndrome, cirrhosis of the liver and psychopolyneuritis. It occurs in heavy drinkers who mix their liquors, and has a predilection for the female sex. After some years of alcoholism the picture of cirrhosis of the liver may develop or the initial symptoms may be nervous. The physician is first consulted for disturbance of gait or other symptoms due to polyneuritis. The lower extremities show the greatest participation, although as a rule all 4 limbs are involved. Ocular paralyses are common and tachycardia is the rule. In regard to the liver hypertrophic cirrhosis is the form usually seen. The psychic disturbances comprise amnesia, mental confusion, and dream states. The course is rapid and prognosis bad, especially in women. Donnet (*Presse Méd.*, Mar. 1, 1917).

#### DIFFERENTIAL DIAGNOSIS.

—The preceding pages will have given in fairly full detail the main features characterizing the different forms of hepatic cirrhosis. As shown below, however, there are five hepatic disturbances, between which we have to

distinguish, namely: portal cirrhosis proper, biliary cirrhosis of the Hanot type, obstructed biliary cirrhosis, chronic perihepatitis, and gummatous syphilis of the liver. All other forms, with the exception of the pericellular syphilitic cirrhosis of the infant, are clinically unrecognizable.

Leaving aside, for the moment, the most important of these—namely, portal cirrhosis—the main features whereby Hanot's cirrhosis is to be differentiated are the progressive icterus, the enlargement of the organ, the absence of marked digestive disturbances, the long continuance of the condition, and the retention of appetite and strength. The coloration of the stools by bile and the more extensive enlargement of the organ must be the main factors in diagnosing between this and the rarer purely obstructive form.

**Gummatous syphilis** is only likely to be confounded with portal cirrhosis when, through obstruction to the portal circulation, ascites supervenes. Under these conditions the organ may be either of normal size or greatly contracted by a multitude of syphilitic cicatrices. In the former case the coarse lobulation of the organ is more likely to lead to the diagnosis of cancer of the organ than of portal cirrhosis; in the latter case the signs and symptoms may be so closely allied to those of portal cirrhosis as to render diagnosis a matter of extreme difficulty. The presence of syphilitic lesions elsewhere and the history of the case may help the diagnosis, which will be finally determined by the effects of antisyphilitic treatment.

**Generalized fibroid perihepatitis** may, with great difficulty, be distinguishable from true portal cirrhosis. If the organ can be felt, the rounded character of the edge, the absence of rough-

ness of fine nodulation on palpation, the presence of a thickened omental mass below the liver, all are in favor of a diagnosis of perihepatitis. As already stated, according to Hale White, if a patient is able to stand a long series of tappings of the ascitic fluid, the diagnosis is against the existence of an uncomplicated portal cirrhosis, and is in favor either of chronic peritonitis associated with perihepatitis or of portal cirrhosis complicated by chronic peritonitis.

The main points elicited in the preceding pages with regard to portal cirrhosis and its diagnosis are the following:—

1. That the small size of the organ is by no means the main diagnostic feature of this condition. Only in advanced cases, and by no means always then, is the organ markedly atrophied. Of far greater diagnostic importance is the determination of progressive diminution in size of the organ.

2. If the organ be palpable, the recognition of a finely nodular, firm surface indicates with relative certainty the existence of this condition.

3. Contrary to general opinion, in only about 50 per cent. of the cases in which the autopsy reveals a well-developed condition of portal cirrhosis is there ascites.

4. Enlargement of the spleen of medium grade is a much commoner symptom, and this is present in more than 80 per cent. of the cases.

5. Jaundice is present in about 30 per cent. of cases. Such jaundice tends to be transient and to develop after other symptoms have been present some little time.

6. From the very onset of the condition gastric and intestinal disturbances form a prominent feature in the disease.

7. The progressive emaciation and weakness are also characteristic, and with this may be associated a peculiar, sallow, slightly earthy complexion.

8. A urine free from sediment (mainly of urates) is against the diagnosis of cirrhosis, while the presence of increased quantities of urobilin is, in the presence of other symptoms, in favor of such a diagnosis.

Of other conditions affecting the liver which may be confounded with cirrhosis are to be mentioned cancer, thrombosis of the portal vein, senile or marantic atrophy of the liver, and cyanotic induration.

Of these, **portal thrombosis** may occur as a complication of cirrhosis. Where this occurs in the absence of cirrhosis the main distinguishing feature is the rapid development of the ascites and its rapid return after tapping. At the same time, such thrombosis is secondary to disease of other abdominal organs, more frequently of the intestinal tract, and the symptoms proper to such disease will have preceded the development of ascites.

**Secondary cancer of the liver** is characterized by the increase in size of the organ, the presence of large nodules presenting umbilication, the absence of splenic enlargement, the cancerous facies, and, in general, the presence of cancerous nodules elsewhere. Those cases in which cancer of the organ is present without the development of nodules upon the anterior surface of either lobe at times cause very great difficulty. Here the small size of the spleen, the character of the urine, the complexion, and other signs and symptoms which ordinarily are regarded as of secondary importance become of the highest value in diagnosis.

In cases of **senile**, or **marantic**,

**atrophy** the organ, if it can be palpated, is smooth; there is absence of ascites and of jaundice.

The **atrophic nutmeg liver** (cyanotic induration) and also the "hypertrophied" nutmeg liver are also characterized by the smooth surface of the organ, as also by the prominent symptoms of obstructive disease of the heart.

Other forms of ascites and peritonitis are not infrequently mistaken for the results of cirrhosis; indeed, I think it may be said with confidence that the most frequent cause of false diagnosis of cirrhosis is either **cancerous** or **tubercular peritonitis**. In such cases there may be present gastric and intestinal disturbances easily mistaken for those accompanying cirrhosis; the ascites may be of gradual development, as in portal cirrhosis, and the liver, being by the accumulation of fluid, forced upward, may disappear behind the ribs and so be diagnosed as presenting great atrophy. Between cancerous and tubercular peritonitis the distinction may be drawn that in the former the spleen is not enlarged, and in the latter the enlargement may be as extensive as in portal cirrhosis. In these cases, again, it is the secondary symptoms and signs which are of the greatest value in arriving at a decision: complexion, urine, etc., and, in addition to these, the character of the abdominal fluid when removed. Most important, also, are manifestations of disease elsewhere, either cancerous or tubercular. In cases of doubt, to determine the tuberculous nature of the condition, it is well to inoculate a rabbit or guinea-pig, and, for the recognition of cancer, to make a careful search for cancer-cells in the removed fluid.

**COMPLICATIONS.**—Leaving out of account the rare cases of develop-

ment of a primary adenomatous or cancerous condition, there may be other complicating conditions in the liver itself of the nature of degenerative changes; in advanced cases it is not infrequent to meet with evidence of fatty degeneration of the cells as distinct from the fatty infiltration seen in less advanced conditions; more rarely is amyloid degeneration present. Thrombosis of the portal vein occurs occasionally.

**Tuberculosis.**—The most frequent complication outside the liver is the development of tuberculosis. Rolleston and Fenton find pulmonary tuberculosis in 32 out of 114 cases, tuberculosis being the direct cause of death in 17. Kelynack, out of 121 cases, finds tuberculosis either active, latent, or obsolete in 28, *i.e.*, 23 per cent. Of these 28, in 14 the condition was active in the lungs, in 12 in the peritoneum, and in 7 both in the lungs and peritoneum. Twelve, or about 10 per cent., of the cases died directly from tuberculosis; in 8 per cent. the condition was latent or obsolete.

The tuberculous infection acts on the liver as on the lung, sometimes inducing ulcerative lesions and sometimes merely sclerosis. In his patient there had evidently been a slow circumscribed chronic process; the liver was enlarged, hard, and sclerotic. As this circumscribed process began to spread, an acute process developed, a parenchymatous reaction with fatty degeneration and atrophy. This assumption corresponds in every particular to the symptoms exhibited by the patient and the anatomical findings.

These findings indicated a chronic tuberculous affection of the pleura, with recent invasion of the peritoneum, as the liver diminished in size. Vincenzo (*Riforma Medica*, Nov. 16, 1904).

The writer studied systematically the livers from 120 guinea-pigs inoculated with tubercle bacilli, and finds quite constantly definite cirrhotic changes which correspond in a certain way to cirrhosis of the liver in man. In this series of cases the bacilli evidently reached the liver through the portal veins or lymphatics, for the earliest changes were found about the intrahepatic branches of the portal vein. These consisted in a proliferation of epithelioid cells and new formation of young connective tissue. At this stage of the process marked proliferation of the liver bile-ducts can be seen, with transitions between the bile-ducts and columns of liver-cells. As the lesions grow older, the picture of a tuberculous infection becomes less characteristic, the proliferation of the portal connective tissue becomes prominent, and the new bile-duct formation is extensive. Usually the ramifications of the portal vein are narrowed or occluded by the connective-tissue growth and, owing to this, foci of necrosis are formed in the liver parenchyma. The necrosis in turn leads to further proliferation of connective tissue. Finally, in the most advanced stages of the process, signs of tuberculous infection have entirely disappeared, and the liver presents an appearance not unlike that seen in portal cirrhosis in man. In contrast to this nodular type of cirrhosis, another form, comparable to the biliary cirrhosis, was met with in which the liver was large and smooth, and showed on section almost complete disappearance of the normal liver-cells. Stoerk (Wiener klin. Woch., Bd. xx, S. 847, 1907).

Chronic tuberculosis is capable of producing in man changes in the liver anatomically identical with those of cirrhosis. Clinically there is usually lacking direct evidence of diseased liver, since the liver condition is masked by the chronic tuberculosis. This is particularly true because in these cases there is apt to be peritoneal tuberculosis with ascites. The

symptoms, common in alcoholic cirrhosis, such as pain in the hepatic region and icterus, are usually lacking in the tubercular cases. Reports of a case in which the clinical diagnosis of tuberculosis of the pleura and peritoneum with probable tubercular cirrhosis was made. At autopsy the liver showed changes which the author regards histologically as beginning cirrhosis with scattered tubercular nodules. Jagic (Wiener klin. Woch., Bd. xx, S. 849, 1907).

The writer has succeeded in reproducing in guinea-pigs all the various processes of human tuberculous hepatitis. Some of them were reproduced to their finest details, especially the forms of cirrhosis with hypertrophy and atrophy. All the evidence presented confirms the rôle of the tubercle bacillus in the development of such affections in man. The tuberculous nature of certain forms of cirrhosis is fully established by the research related, in which he inoculated animals with pure cultures of the tubercle bacillus and cirrhosis of the liver developed in consequence, the series being too numerous to be ascribed to mere chance. The experiments show that the tubercle bacillus alone, without the aid of alcohol, is able to induce typical cirrhosis of the liver. Gougerot (Revue de méd., Feb., 1909).

The writers conclude, after a study of 20 cases, that the ascites of cirrhosis of the Laennec type is always of tuberculous nature, and implies the presence of an inflammatory process involving the peritoneum. G. Roque and V. Cordier (Revue de Méd., Dec., 1912).

Other frequent complications are: **right-sided pleurisy** with a serous or serosanguineous exudation. This condition has not, as yet, been thoroughly worked out; so far as I can see it is not of a tuberculous nature, for I have come across cases showing such pleurisy in which there has not been a sign of tuberculosis at the *post mortem*.



Where it is present I have also noted a coexistence of adhesions between the upper surface of the liver and the diaphragm, which might indicate an extension of the inflammatory process from the liver to the pleural cavity. Were this so, it would be evidence in favor of microbic origin or microbic complication in the hepatic condition; but, as already stated, this subject requires much further study. Occasionally there is evidence of bilateral pleurisy.

Analysis of 25 cases of pleuritic effusion on the right side due to heart disease and cirrhosis of the liver studied at the autopsy table after the writer had seen the patients in the hospital. He draws the following conclusions from his own observations: Effusions in the pleura on the right side are frequently met with in heart disease, especially in the last stages, with cachexia and heart weakness. These effusions occur more often in heart affections due to arteriosclerosis than in valvular disease. The inflammatory nature of the exudate could be demonstrated in the majority of the cases analyzed, and this was in conformity with the views of the French school, as well as those of Villani, although other Italian clinicians, led by Bacelli, assert that these effusions are mechanical in origin. Giauni (*Gaz. degli Ospedali*, April 2, 1905).

Another not uncommon, but still not frequent complication is **nephritis**, either of the granular type or not infrequently as a mixed interstitial nephritis of what Formad has termed the "hog-backed" type, the organ being enlarged, more especially from before backward, and showing microscopically a condition of mixed interstitial and parenchymatous nephritis. The interstitial type is, in general, associated with evidences of some degree of general arteriosclerosis and with other

complications due to this process. Both the interstitial and the hog-backed kidney are, it need scarcely be said, characteristic of alcoholism. The statistics of the various authorities with regard to the frequency of renal complications are not sufficiently extensive to arrive at any very satisfactory conclusion. G. Foerster, in his 31 cases recorded at Berlin, found nephritis 3 times, granular atrophy 4 times, and "indurated" kidney 4 times. Kelynack found renal cirrhosis in a little over 18½ per cent. of his cases. Gärtner found 11 out of 12 to show "chronic nephritis"; 10 of these were habitual drinkers of brandy.

Other alcoholic complications may also be present, notably some extent of chronic pachymeningitis and thickening of the dura mater, and fatty degeneration of the heart muscle, as, again, indications of chronic esophagitis, and notably the presence of esophageal leucoplakia, or the presence of multiple whitish plaques of hypertrophy of the esophageal epithelium.

In 3 cases of pure alcoholic cirrhosis of the liver without tuberculosis or arteriosclerosis, the writer found at autopsy the heart diminished in size and weighing, respectively, 125, 150, and 183 Gm. (4, 5, and 6 ounces) instead of the average 250 Gm. (8 ounces). In the last case the wall of the left ventricle measured 10.5 mm. instead of 12 mm., and the circumference of the aorta 57 mm. instead of about 65 mm. The small size is readily made out by percussion *intra vitam*. The existence of renal or arterial disease is the exception; when present, causing hypertension and cardiac hypertrophy. The small size of the heart must be in relation to the hypotension in the arteries, as pointed out by Gilbert and Garnier. Both are dependent upon the hepatic obstruction, which causes a portal hypertension and a diminution in the volume of blood coursing

through the heart in a given time. Carnot (*Progrès méd.*, vol. v, p. 61, 1909).

Lastly, there is a liability for acute inflammatory processes to supervene: pneumonia, acute bronchitis and pericarditis, erysipelas of the edematous skin, and acute peritonitis; this last often secondary to paracentesis.

**ETIOLOGY.**—This form of cirrhosis is most frequently associated with alcoholism, more especially with the use of spirits, and as a consequence has become known in England as the *gin-drinker's liver*. At the same time a small proportion of cases is met with in which there is an entire absence of the alcoholic history.

Upon this continent all other causes are insignificant when compared with the one prime cause of excessive and long-continued use of alcohol.

Analysis of 54 cases from the writer's practice showed that alcohol was unmistakably to be incriminated in 59.25 per cent. In the other cases alcohol could not have been a factor, but infectious diseases, malaria, syphilis, etc., tobacco, lead poisoning or thyroidism evidently had a share in the morbidity of the liver. Martinez (*Prog. de la Clinica*, Aug., 1918).

While this is the case and while alcohol must be regarded as a prime cause, much evidence has accumulated of late years to throw doubt upon alcohol as the primary cause. As Payne has pointed out, cirrhosis of the liver is the exception and not the rule in autopsies upon drunkards; the fatty, and not the cirrhotic, liver is typical of alcoholism. In 250 autopsies upon confirmed alcoholics dying suddenly, Foxwell encountered cirrhosis in 6 cases only. Besides this, the experiments of a large number of observers have failed to demonstrate that ethylic, and not amylic, alcohol is

capable of producing any marked development of cirrhosis in the livers of rabbits, dogs, pigs, or rats. In fact, only two observations, those of Straus and Blocq in the rabbit, and of de Rechter in the dog and rabbit, have afforded such cirrhotic changes. Magan, Ruge, Pupier Naire, Combemale, Strassmann, Afanassijew, von Kahlden, Lafitte, and Kerr have found almost entire absence of portal inflammation, but have noticed more or less extensive fatty infiltration and fatty degeneration.

It may be urged that these observers did not preserve their animals for a sufficient length of time; nevertheless, several of the observers kept their animals for several months, and, were alcohol the direct cause of the disease, there should undoubtedly have been more evidence of, at the least, a beginning inflammation in the portal sheaths around the lobules.

This discrepancy between the experimental results and the history given in man of alcoholism is to be explained in two ways: Either it must be admitted that alcoholism is the primary factor in cirrhosis, in which case it has to be acknowledged that individual predisposition plays a part of almost equal importance; so that cirrhosis is to be described as being due to the fibrotic or cirrhotic diathesis manifesting itself under the influence of alcohol. Or, on the other hand, we must regard alcohol purely as a predisposing cause, and must pass beyond the alcoholism and admit that, at most, alcohol causes irritation and inflammation of the gastric intestinal mucosa, whereby either toxic substances pass into the portal blood from the intestines (and regard these toxic substances as the direct cause of the inflammatory condition of the organ), or it is possible to go further and

regard the inflammation as set up by some form of micro-organism entering the liver along the same paths. Upon the whole, the toxic, as opposed to the direct alcoholic, view would appear to be the more correct.

Rolleston, following Budd and Young, called attention to the cirrhosis of Hindoos, and notably of the Brahmins, who never touch alcohol and lead abstemious lives save that they are addicted to ginger, cardamom, red pepper, and other hot and irritant spices. These may well induce dyspepsia, intestinal irritation, and abnormal fermentation.

Various poisonous materials circulating in the blood may cause the destruction of the cells of the liver, sometimes in very small foci, sometimes much more diffusely, throughout the whole organ. When the injury is limited in extent it may destroy so little of the liver that no definite symptoms result, and the injured area is in time replaced by scar-tissue. But if the injury is very extensive and involves at one time the greater part of the liver, symptoms at once arise, and such a condition, which is commonly classed as acute yellow atrophy, may quickly bring about the death of the patient. But there may occur a scarred condition of the liver perhaps intermediate between the ordinary cirrhosis and an extraordinary distortion, a condition in which some single attack of an infectious disease or some single intoxication has produced a single non-progressive, though widespread, injury from which complete and permanent recovery has occurred. W. G. MacCallum (*Jour. Amer. Med. Assoc.*, Sept. 29, 1906).

Two cases of hepatic cirrhosis in young subjects. Both began insidiously with all evidences of a simple catarrhal jaundice and were so looked on until considerable and rapidly increasing enlargement of the liver showed that they were of more seri-

ous nature. In both, jaundice was very marked. In both, the liver shrank rapidly in size as the symptoms of grave icterus developed. In one patient this condition developed abruptly and terminated in death in the surprisingly short time of thirty-six hours. In the other patient the development was somewhat less abrupt and the duration several days. In both, the terminal clinical pictures most clearly resembled acute yellow atrophy. The pathologist showed that both these cases were instances of hepatic cirrhosis. Mitchell (*Ohio State Med. Jour.*, Nov., 1910).

According to the writer, hepatic cirrhosis of malarial origin is due to the formation of fibrous tissue primarily around the bile capillaries and single lobules of liver tissue, and the presence of adhesions in the transverse fissure, thickening of the walls of the gall-bladder, and swelling of the neighboring lymphatic glands. The sequence of changes appears to be: (1) The formation of adhesions and enlargement of the lymphatics, pressing upon the bile duct; (2) the swelling of the liver at each attack of malaria; (3) as the adhesions and perihepatitis increase the organ is held as in a vise; (4) thus there is an increased internal pressure, acting against pressure on the bile ducts and in the gall-bladder; therefore, fibrous tissue is formed around the bile capillaries as a compensatory act; (5) malarial "toxines" are formed in the liver, and being excreted under unusual pressure along the bile capillaries, add a further irritating factor. The deleterious products which should normally be excreted with the bile are absorbed into the system, and cause the enlargement and profound changes that take place in the spleen. L. Nicholls (*Jour. of Trop. Med. and Hyg.*, June 2, 1913).

All these are cases of disease possessing a similar character, namely: characterized by the development of the inflammatory new tissue in the portal

sheaths and more especially around the branches of the portal vein. For the present time I leave out of account the other forms of cirrhosis which are of a different type brought about by other toxic agents and the consequent development of inflammatory foci or focal necroses irregularly scattered through the liver-substance.

Eight cases illustrating the bond that unites the pathology of the liver to that of pancreas. They showed that the pancreas is often injured in cases of hepatic cirrhosis of venous origin, the injury showing itself as a sclerosis, with participation of the glandular parenchyma. The same kind of a process thus affects the two organs in a similar manner. The most frequent lesion of the pancreas is an intralobular sclerosis which gives the appearance of fibrous plates developed in the midst of the lobule and radiating toward the interlobular connective-tissue trabeculae, breaking the lobule up into groups of 10 to 20 acini. This form of sclerotic lesion is usually combined with a periacinous or monoacinous sclerosis in which each acinus is clearly isolated from the neighboring acini by a connective-tissue interval. In other cases there is an interlobular or perilobular sclerosis which is an increase in size of the connective-tissue trabeculae that separate adjacent lobules in the normal state. The islands of Langerhans appear to resist this process better than do the glandular acini. Klippel and Lefas (*Revue de méd.*, Jan. 10, 1903).

In a series of studies on the alterations produced in the pancreas by cirrhosis of the liver, the pancreas showed a growth of interstitial connective tissue circumlobular in location, but this increase is not found uniformly in all cases—at times it is quite diffuse, invading the lobules, and in other cases the tissue remains circumlobular. In no case was the growth of interstitial tissue very marked. The islands of Langerhans

also participate in the morbid process, but the changes in these are not very marked. Sometimes they consist merely in an enlargement of the epithelial cells, but at times there is a true inflammation in the islands, or they are surrounded by connective tissue. In addition, there are noted in the pancreas in cirrhosis marked hyperemia of the passive order, hemorrhagic infarcts, and diffuse necrosis. There is, besides, some fatty degeneration, which is not constant. The chronic inflammatory changes described are not due to the hyperemia, but to the same cause as the cirrhosis. The changes in the pancreas in cirrhosis explain the occurrence of diabetes in patients with cirrhotic livers. D' Amato (*Riforma Medica*, Sept. 16, 1903).

The pancreas studied in 23 cases of cirrhosis of the liver. In most instances the cirrhosis was of atrophic type and in 15 cases there was a history of alcoholism. Diabetes was present in 3 instances. The pancreas in all cases showed more or less overgrowth of connective tissue, which in 12 cases was about proportionate to the cirrhosis of the liver. The pancreatic cirrhosis was at times entirely intralobular and confined to the interacinar connective tissue; at other times the increase was principally in the interlobular connective tissue, though in this type there always existed some increase in the intralobular connective tissue too. The head and tail of the pancreas seemed to be affected first and exhibited the most extensive changes. In a case of pigmentary cirrhosis of the liver there was also marked pigmentation of the pancreas. The islands of Langerhans presented usually some alterations, which, however, except in the cases of diabetes, were marked neither in degree nor extent and consisted in slight thickening of the capsule or vessels and degenerative changes of the epithelium. In 2 of the cases of diabetes there was hyaline degeneration. Increase or thickening of the elastic tissue of the

organ was often noted. The weight of the pancreas varied from 32 to 150 Gm. The form of the cirrhosis, whether atrophic or hypertrophic, made no difference in the microscopic picture of the changes in the pancreas.

Two principal causes for the lesions in the pancreas are discussed. It is possible, first, that the changes in the pancreas may be the sequence of a chronic passive congestion following the cirrhosis of the liver, or, secondarily, the etiological factor in the production of the cirrhosis of the liver may also cause the changes in the pancreas. Lando (*Zeitsch. f. Heilkunde*, Bd. xxvii, S. 1, 1906).

Case in a child 2 years old, in whom symptoms of cirrhosis of the liver developed and proved fatal in less than a year. The necropsy findings confirmed the assumption of inherited syphilis. Mercurial treatment came too late; the liver had been already irremediably damaged. O. Pentagna (*Pediatrics*, Mar., 1917).

**Age and Sex.**—With regard to sex, the condition affects males more than twice as frequently as it does females; indeed, some authorities would make it as much as three times more frequent in males. From the more recent statistics of Rolleston and Fenton, and of Kelynack, it would appear that the most common age at which death occurs is between 40 and 50; two-thirds of the fatal cases occur between 35 and 50. Rolleston gives the average age in males having an alcoholic history as 48, without alcoholic history, 49, and in females 46 and 51, respectively. Kelynack gives the average of his 121 cases as: males, 45½; females, 42. But the condition may develop at almost any period of life; numerous cases have now been brought forward in children since Palmer Howard published his classical article on this subject.

Case of alcoholic cirrhosis in a boy of 4 years which does not seem classifiable into any of the classes of

cirrhosis usually given. The child was the first of healthy parents, and in good health until last June. The onset of his illness was indefinite, but he grew slowly, but steadily worse. In October, when the writer saw him, he presented no abnormality, excepting that his liver was symmetrically enlarged nearly down to the level of the umbilicus in the midclavicular line. The spleen was not palpable. The surface of the liver was even and smooth, and there were never any irregularities felt. There was no jaundice and no history of any; none developed later. The liver continued to enlarge until the time of his death, on November 25, 1909, when it extended about an inch below the umbilicus in the midclavicular line. There was increasing anorexia, but no disturbance of digestion. The urine showed concentration, excess of urates, and the slightest possible trace of albumin. During the last two weeks of the child's life there was slight edema of both upper and lower extremities. There was no palpable ascites and the spleen was at no time palpable. The cause of this enlargement was not apparent until it was learned that the father was accustomed to have beer and whisky, and it seemed that from the time this child was able to drink from a glass he was given some with the others. This probably continued over a period of nearly two years, but the amount taken at any one time was never large. It might be of the "fatty" class described by Osler. Blakely (*Boston Med. and Surg. Jour.*, Feb. 24, 1910).

Case of cirrhosis of the liver in a boy of 12 years. The liver affection developed very gradually, with enlargement of both the spleen and liver, slow fever and some jaundice, swollen lymph-nodes, tendency to hemorrhage, and arrest of growth. The boy has not grown during the eight years since, his appearance being still that of a boy of 12. The primary cause is a mystery, as neither inherited syphilis, malaria, nor alcohol can be incriminated. The young

man now shows signs of tuberculosis, but it seems to be secondary. Pagliano and de Luna (Annales de méd. et chir. infantiles, April 1, 1912).

**PATHOLOGY.**—In alcoholics, in whom the condition most frequently develops, the liver is, at first, large, owing to the fatty infiltration and hepatic congestion, both of which are the direct result of alcoholism. In what is taken to be the earliest stage there is observable an abnormal collection of small, round cells infiltrating the portal sheaths and causing them to stand out prominently in the stained sections, the greatest accumulation being in the neighborhood of the vessels running in those perilobular sheaths. In somewhat more advanced conditions the sheaths have undergone definite enlargement and are formed of dense, fibrous tissue, although there is still an abundant infiltration of small, round cells, more especially at the margins where they abut upon the lobular parenchyma. Just as at the beginning the infiltration is not evenly distributed around the lobules, so in more advanced conditions the development of fibrous tissue is not even, and as a consequence the newly formed bands of fibrous tissue tend to surround many lobules; the fibrosis is what is termed *multilobular*.

It is this appearance in the portal sheaths seen in what are regarded as the slightest cases of the condition that is the justification for speaking of this as portal cirrhosis. It must be clearly understood that in advanced cases the fibrosis is no longer recognizable as associated with the portal sheaths. There is, in fact, extraordinary irregularity. The individual lobules are difficult to recognize and greatly distorted, and often what are surely intralobular branches of the

hepatic vein are found not in the center of a mass of hepatic cells, but at the periphery, enclosed to a greater or less extent by the new connective tissue. This arrangement or want of arrangement is in harmony with Opie's observation, that not the peripheral, but the central, cells of a lobule may have undergone the greatest destruction.

As this inflammatory new connective tissue reaches maturity, it contracts and by its shrinkage is produced the nodular and hobnailed surface of the organ. In regions or cases in which this process of connective-tissue formation has reached its limit or is not progressing, the new bands are sharply defined from the included parenchyma of the organ; where it is continuing to advance there is not the same sharp separation; small groups of liver-cells at the periphery of the lobules may be seen more or less surrounded by strands of newly forming fibrous tissue and exhibiting well-marked signs of atrophy.

There is still much debate as to whether of necessity the first stage of portal cirrhosis is characterized by enlargement of the organ. Some recent writers, including Osler, would draw a distinction between the ordinary atrophic and the fatty cirrhotic liver. It is true that patients may die of intercurrent disease when the liver is still enlarged and fatty, and that, on the other hand, patients may only exhibit symptoms of cirrhosis when the organ is already so contracted as to be scarcely, if at all, palpable. But, taking into consideration the direct effects of alcoholism and calling to mind three or four cases in which, by good fortune, careful notes of the size of the liver were taken during the months preceding symptoms of portal obstruction, I

cannot but uphold the view that portal cirrhosis (where associated with alcohol) has a preliminary stage of hepatic enlargement. Where alcoholism is not intimately connected with the development of the condition there, such preliminary enlargement may not, of necessity, form a stage in the development of the condition.

The most noteworthy fact in the study of cirrhosis is the complete rearrangement of the architecture of the liver parenchyma. Some liver lobules are entirely destroyed, while, on the other hand, there are positive evidences of regeneration and hyperplasia of liver-cells. The only apparent difference between the new lobules and normal liver-tissue is in the arrangement of the cells and the relation of the capillaries and central veins. This arrangement of cells and lobules is followed by fibrosis, which contracts and atrophies the liver-cells and obstructs and obliterates certain interlobular and intralobular branches of the portal vein. Kelly (*Amer. Jour. Med. Sci.*, Dec., 1905).

Experiments upon repair processes in the liver, following hepatic degeneration produced by injections of hemolytic immune sera. The author found in previous work that focal necrosis of the liver, due to the formation of red-blood-corpuscle thrombi, followed intravenous injections of hemolytic immune sera. In order to study the repair processes in the liver, dogs were injected intravenously or into the abdominal cavity with serum obtained from rabbits which had received repeated doses of red blood-corpuscles of dogs. The dogs which did not die within forty-eight hours of the injections were killed at intervals of from forty-eight hours to thirty-six days. Of these there were 15. The writer found in the livers of these dogs a definite and constant chronic hepatitis, which is more definitely a cirrhosis than any experimental lesion thus far produced. In the dogs allowed to live longest after

the injection, broad bands of connective tissue were found replacing the necrotic areas, in which islands of surviving liver-cells were found about the portal spaces.

The author does not consider that the lesion is analogous to cirrhosis of the liver in man, except that form following chronic passive congestion, but he considers it important in explaining the histogenesis of cirrhosis and repair processes in the liver in general. His experiments definitely show, however, that cirrhosis of the liver may follow extensive primary destructive lesions, and he supports the idea that cirrhosis of the liver is a reparative process. R. M. Pearce (*Jour. Exper. Med.*, vol. viii, p. 64, 1906).

It is remarkable how extreme may be the atrophy of the organ as a result of this fibroid contraction. Cases are on record in which in place of the normal 50 to 60 ounces (1500 to 1800 Gm.) the organ has weighed from 16 to 10 ounces (480 to 300 Gm.) and even less, and notwithstanding this the main symptoms of the disease may not be referable to the diminished activity of the organ so much as to the secondary disturbances of the portal circulation. Despite the great development of contracting fibrous tissue around the lobules, bile may yet find its way from the bile-capillaries into the bile-ducts, and the fibrous bands, instead of appearing to be anemic, appear to possess abundant blood-capillaries. Obstruction there is to the portal circulation, and yet these capillaries can be easily injected from the portal vein, so that it is not necessary to assume, as some have done, that the blood-supply of the liver in this form of cirrhosis is, in the main, conveyed by the branches of the hepatic artery. As a result of the process, the organ is dense, firm, and of almost leathery consistence, present-

ing, on section, minute islands of reddish-yellow parenchyma of varying size surrounded by the more glistening bands of connective tissue. If the condition be complicated with jaundice, then the islands of liver-tissue more especially are tinged by the bile-pigment; if with hemochromatosis (pigmental cirrhosis), both fibrous and liver-tissue may show a darker, slaty tinge; if the liver-cells still retain a fair amount of fat the islands of parenchyma appear of a paler yellow; if the process has been of more acute development, then with the fibrosis there may be inflammatory congestion, and the organ, in general, have a reddish appearance.

In general, the left lobe is more affected and more shrunken than the right; sometimes it is singularly small,—a mere appendage to the larger right lobe; but this is not constantly the case, and the opposite may occur. It must be kept in mind that the right lobe may be contracted behind the ribs and the left still be prominent: a condition which has more than once led to the mistaken diagnosis of hepatic or pancreatic tumor.

**PROGNOSIS.**—The condition begins so insidiously that it is difficult to make an accurate statement concerning its duration. It will be generally agreed that Fitz is not too hopeful in stating that the fatal result may be expected within a year after hemorrhage or other sign of portal obstruction.

Von Kahlden has reported a case of very acute development of the disease in which death occurred three and a half months after the first symptoms presented themselves. The form of cirrhosis in this was of a mixed type. If the cases of Carrington and Cayley are

to be regarded also as examples of portal cirrhosis, we have further evidence that the disease may be fatal in three months after the first occurrence of dyspepsia and of epigastric fullness, or two months after the first onset of ascites. At the other extreme, we come across many cases, in the post-mortem room, of well-developed portal cirrhosis which had given rise to no symptoms during life. Thus, clearly the condition may be present in an arrested form for months and it may be for years. It is difficult, also, to know how to regard those cases in which, cirrhosis being diagnosed, after one or two tapings the symptoms disappear and the patients apparently recover, because these cases may have been conditions not of true cirrhosis, but of subacute perihepatitis. If, by palpation and by other physical signs and symptoms, and more especially by the character of the urine, it is determined that portal cirrhosis is present, prognosis is very bad.

Both Rolleston and Kelynack agree that a little under half the cases die directly from the effects of hepatic cirrhosis, though it is a little doubtful what effects they include under this term.

A relative increase in the leucocytes in cirrhosis is of great and immediate prognostic value. Of a total of 15 cases showing an actual or relative leucocytosis, 60 per cent. ended fatally in a short time, while other patients were discharged without any improvement. On the other hand, in 9 cases without any leucocytic increase the mortality was only 11 per cent. The differential count in the cases having a leucocytosis shows a polynucleosis up to 93 per cent. Rogers takes this as an indication of the development of a terminal bacterial infection, due possibly to *Bacillus coli communis*. Rogers (*Lancet*, Aug. 10, 1912).



## II. HANOT'S CIRRHOSIS.

**Synonyms.**—Hanot's cirrhosis; hypertrophic biliary cirrhosis; infective biliary cirrhosis.

So long ago as 1846 Requin and again in 1857 Todd drew attention to the fact that two different forms of chronic hepatitis are to be recognized, and quoted cases of enlarged cirrhotic liver without ascites, but with jaundice, so that, while Hanot was the first to give a full study of this form, he was certainly not the first to clearly draw attention to its existence. In 1859 Charcot and Luys called attention to the fact that, in some cases of cirrhosis with enlarged liver, the new fibrous tissue penetrates into the lobules and becomes intralobular. In 1874 Hayem reported 2 cases of cirrhosis with enlargement and in the same year Cornil pointed out the presence of great numbers of new bile-ducts in cases of cirrhosis of this nature; only in the following year, in 1875, did Hanot's well-known thesis appear upon the "Enlarged Cirrhotic Liver," in which he pointed out that in this form the enlargement is constant throughout, the surface smooth, and, microscopically, the cirrhosis is of the unilobular type and sometimes pericellular, with a plexus of small, new pseudo-bile-canaliculi; while, clinically, he showed that this form was characterized by permanent jaundice without ascites, death being due to the jaundice. He described the condition as often due to a catarrhal condition of the smaller intrahepatic bile-ducts. The condition is a rare one, though each year two or three cases are reported in the journals.

The liver in these cases may be enlarged symmetrically and may weigh as much as eight pounds (4000 Gm.).

**SYMPTOMS.**—Pain of a dull character is felt in the region of the liver,

with some tenderness. There may be pain of a similar type in the splenic area, and where the splenic enlargement precedes the cirrhosis this may be the first noticeable symptom. While the general health appears to be fairly good and the appetite to be excellent, there is a slight fever and very characteristic is the development of a series of more acute attacks of abdominal pain resembling mild hepatic colic, associated with each of which the jaundice becomes more marked. Most often it is the slight, but persistent jaundice that first leads the patient to seek advice. Gradually the abdomen becomes enlarged, the enlargement being due to the increased size of the liver and of the spleen; the former, on palpation, presents a perfectly smooth surface. The process is, in general, of slow development; only after months may the abdomen become markedly enlarged, and the enlargement may slowly continue for as many as eight years; but the jaundice is progressive and becomes so intense that the skin takes on a dark-green color. The jaundice is not obstructive, as shown by the fact that the stools continue to be stained. The urine, according to Hanot, shows slight diminution of the urea, is high colored, and contains abundant pigment. Throughout the disease there is absence of marked ascites, though in some cases there may be evidences of intestinal hemorrhage. Sometimes there is a little fluid in the abdomen, and where this is the case it would seem to be associated with the development of perihepatitis and perisplenitis. Where eventually marked ascites supervenes there may be found at autopsy a mixed cirrhosis, the liver presenting a more hobnailed character, with some atrophy and more irregular disposition of the bands of connective

tissue being found upon microscopic examination eventually, that is, a portal cirrhosis becomes implanted on the biliary.

As the disease progresses, there is loss of strength, and with the progressive emaciation petechiæ may show themselves. Finally coma supervenes, and death occurs directly from the hepatic disturbance.

A little-known symptom which may occur in biliary cirrhosis is clubbing of the fingers, similar to that which may occur in chronic pulmonary and cardiac diseases. The writers first drew attention to it in a case of infantile biliary cirrhosis in 1895. Since then about 40 cases have been reported, in most of which no respiratory affection existed, and when present was not of sufficient severity to account for the clubbing. This occurs in no other form of hepatic cirrhosis. The soft parts of the finger are especially involved, probably the only part implicated in most cases, but bony changes may occur, as in a case reported by Chatin and Code, in which the phalanges of the index, middle, and ring fingers were swollen at their free ends and studded with osteophytes. The writers regard the digital condition as being due to toxic infection and cholemia. Gilbert and Lereboullet (*Gaz. hebdomadaire de méd. et de chir.*, 1, 2, p. 1, 1902).

In hypertrophic cirrhosis of the liver of uricemic origin there never occurs disturbance of biliary or blood circulation, nor icterus or ascites. The abdominal veins, the portal vein as well as the cava, present no indication of increased pressure or of the *circulus inversus*. The pressure of palpation is disagreeable to the patient, but there is usually only very little pain. There is but a sense of heaviness in the right hypochondriac region. When the patient is in the erect posture the liver prolapses on account of its weight, and it broadens out in transversal direction toward the umbilicus at the same time. The

bulk of the organ is often so great that it produces a pronounced convexity of the last ribs of the right hypochondrium. Thus an inspiratory friction may be called forth which is noticeable by the patient and the palpating hand. The hemorrhoidal veins are slightly engorged; the sphincters have lost some of their contractibility. This uratic form of hepatic cirrhosis differs from fatty degeneration of the liver in so far as in the latter the border remains soft and never attains the peculiar toughness of the former. It is easy to differentiate between carcinoma of the liver and Banti's disease. Baccelli (*Gaz. degli Ospedali*, No. 23, 1908).

Thus, clinically the distinctions between this form of cirrhosis and ordinary portal cirrhosis are:—

1. The earlier life-period at which the disease develops.
2. The enlargement of the liver and its smooth, or but slightly roughened, surface (from perihepatitis).
3. The persistent jaundice.
4. The characteristic exacerbations of hepatic pain and of jaundice.
5. The absence of any marked ascites and of portal obstruction, save at the very end.
6. The preservation for a long period of an excellent appetite.
7. The pronounced splenomegaly.
8. The long continuance of the condition after the recognition of the first signs of hepatic disturbance (often for five and it may be for as long as ten years), and, associated with this, the retention of bodily strength and the slow emaciation.

It is all the more necessary to keep these distinctions in view, inasmuch as, brought about by the indiscriminate employment of the term "hypertrophic," there is the painful confusion between this true biliary cirrhosis and those cases of portal cirrhosis in which there is the

enlarged liver, either of the fatty type or again of the mixed. Nothing has more conduced to confusion with regard to cirrhosis than the employment of this term, and of the relative term "atrophic."

[Strictly speaking, the term *hypertrophy* of the liver should be employed to indicate an overgrowth of the specific liver-tissue, —i.e., of the parenchyma,—but ought never to be employed to indicate the overgrowth of the connective tissue of the organ, or the mere fact that the organ is enlarged. In short, he who wishes to make himself clearly understood will do well never to use the term in connection with the liver. Similarly if the term *atrophic* be banished the unity of the various forms of portal cirrhosis will be better grasped. J. GEORGE ADAMI.]

**ETIOLOGY.**—In the first place, there is a marked distinction between this and ordinary portal cirrhosis, in that it affects young adults. By far the greater number of cases are in males between the ages of 20 and 35. Schochman, in the 26 cases which he collected, found that it affected 22 males and 4 females. In many cases there is a definite history of hard drinking; but, as in other cases there has been no alcoholic history, we must conclude that alcohol is not the immediate cause. So, also, malaria is to be eliminated. On the other hand, there is increasing evidence at the present time—not, it is true, absolutely convincing—in favor of regarding this form as definitely of infectious origin. In favor of this view are the following facts:—

1. The febrile character of the disease. As Jaccoud was the first to point out, the fever may reach from 103° to 103½° F. (39.4 to 39.7° C.).

2. The very frequent extension of the inflammation, development of peri-hepatitis, and surrounding adhesions.

3. The not infrequent existence of a mild graded leucocytosis.

4. The improvement brought about by measures directed to reduce a septic state in the liver.

Hanot, in his later communications, was strongly in favor of the infectious origin. On the other hand, no definite micro-organism has been discovered, save that the presence of the colon bacillus has been recognized in the ducts upon more than one occasion. The frequency with which this form may be present in the gall-bladder and larger bile-ducts and there set up mild chronic disturbances is, nowadays, being more and more recognized.

But were the *Bacillus coli* the causative agent, we should expect to find the disease far more common and far more frequently associated with cholelithiasis.

Closely allied to this above variety of cirrhosis is the "pericellular cirrhosis" (*vide infra*): a form definitely associated with infection. Hence, on the whole, from all these considerations I am inclined to regard this provisionally as being a cirrhosis of infectious origin.

Almost all authorities on cirrhosis of the liver agree that it is due to disturbances of digestion and to the action of bacteria of sepsis and their toxins. Kirikoff made the unique observation that staphylococci occur in the blood of patients with Hanot's cirrhosis. The object of the writer's research was to test the theory of infectious origin of cirrhosis experimentally. For this purpose she made systematic injections of cultures of *Staphylococcus aureus* into rabbits (subcutaneously) and examined the livers of these animals. She found that she could produce acute effects on the liver, not only in its parenchyma, but also in the interstitial tissue. These were followed later by the formation of new connective tissue and the degeneration of he-

patic tissue. Dantchakova (Roussky Vrach, Feb. 26, 1905).

Dantchakova injected staphylococci into the blood of rabbits, while Scagliosi fed animals on alcohol, and at the same time injected various bacteria. Scagliosi found cirrhotic changes in the livers of these animals, though other workers had not found any with alcohol alone as exciting cause. Kravkoff injected staphylococci into birds, and produced cirrhosis of the liver. The writer injected cultures of staphylococci (*aureus* and *albus*) into rabbits. An abscess developed at the site of injection in most cases. For control purposes laparotomy was performed in one rabbit in each group experimented upon, and a piece of liver was removed for examination. These animals usually recovered rapidly from the operation. The doses of culture injected were gradually increased. The microscopic examination of the livers of these animals after a four months' period of infection with staphylococci was entirely negative. In none of the animals did a fatty degeneration or a cirrhosis develop. Drzhevetzki (Roussky Vrach, Aug. 19, 1906).

The fact that uniform degeneration of the liver substance takes place in phosphorus poisoning and similar conditions speaks against any differences in the susceptibility of the various portions of the liver to toxins, and, therefore, it must be supposed that in cirrhosis the toxins do not reach all parts of the organ uniformly. Of course, a bacterial origin of cirrhosis could explain these differences in the amount of injury to the organ, for infectious processes very seldom involve an organ uniformly. In some cirrhotoses, such as those of syphilis, for instance, the unequal distribution of the lesions is explained by the microbic nature of the process, but the great majority of cirrhotic processes are toxic in origin and other explanations are required. The simple experiment of passing variously colored fluids

through the veins composing the portal system gives the clue to the explanation, for it is found that the various streams mix but little while on the way to the liver. Any toxin dissolved in the blood of the veins is accordingly unevenly distributed throughout the organ, the angular branching of the portal vein serving to keep the streams apart on reaching the liver. Ribbert (*Deut. med. Woch.*, Sept. 24, 1908).

What is more particularly laid stress upon by many writers as supporting the infectious, or, at least, the toxic, view is the great enlargement of the spleen. Very often the splenomegaly precedes the hepatomegaly. Three varieties are described by some authors (Chauffard) in which (1) splenic enlargement is the first sign; (2) in which spleen and liver undergo synchronous enlargement, and (3) in which hepatic enlargement precedes the splenic. So marked is this splenic enlargement that the organ may attain from four to six times its normal size, whereas the liver is rarely as much as twice as large as usual. We have, in short, it would seem, a succession of cases from simple splenic anemia (and splenomegaly), through splenic anemia with attacks of jaundice, but without cirrhosis, to splenomegaly with cirrhosis, the cirrhosis being of late development.

Case of hypertrophic cirrhosis of the liver with enlargement of the spleen in a child 8 years old. In the greater number of cases during this age the hypertrophy of the spleen exceeds that of the liver considerably. The liver in this case weighed 755 Gm. (25 ounces) and the spleen 520 Gm. (17 ounces). In 27 cases of hypertrophic cirrhosis of the liver with enlargement of the spleen Lereboullet found 16 among children. It is difficult to eliminate the succession in the appearance of the symptoms, but it seems that the enlargement of

the spleen occurred first. The etiology is not known. Hereditary predisposition is not very likely to be the cause, though the mother showed some signs of cholemia. There seems to have been no source of infection, but the starting point is probably to be looked for in gastrointestinal disturbances. The symptoms were classical for this affection. R. Labbe and R. Demarque (*Gaz. hebdom. de méd. et de chir.*, No. 68, 1902).

Then would come the portal type (Banti's disease), to splenomegaly, recurrent and advancing jaundice, and biliary cirrhosis. The enlargement of the spleen is regarded as being of chronic, infectious origin, and Rolleston is of the opinion that the toxic substances manufactured in this organ passing to the liver become excreted, these, like toluylene diamine, setting up an obstructive inflammation of the bile-capillaries and so a condition of jaundice with descending cholangitis. With him we are inclined to argue that the absence of duodenitis and enteritis is against Gilbert and Fournier's assumption of an ascending cholangitis as the most common cause, although admitting that this, when present, might produce similar disturbances in the liver. This view, it will be seen, demands that here, as in portal cirrhosis, the noxa is conveyed to the liver by the portal vein; it supposes that the irritation shows itself more upon the bile-capillaries after excretion than upon the liver-cells themselves. Such a view is calculated to throw light upon the undoubted fact that eventually as the cells become exhausted there is developed a mixed type of cirrhosis with a combination of the symptoms of both biliary and portal cirrhosis. Thus ascites may eventually supervene, edema, esophageal varices, and hematemesis, and contraction of the liver.

There is also the possibility that the cholangitis is not merely of toxic origin, and not ascending, but of what may be termed excretory infective development; in other words, the possibility has to be kept in mind that bacteria in the circulation may be discharged through the liver. The absence of duodenitis and the good effects of drainage of the gall-bladder and of the employment of urotropine, to be presently noted, strongly support this contention. Here I find myself wholly in agreement with A. O. J. Kelly, in his article in Osler's "Modern Medicine," in which he sums up the condition as "a radicular cholangitis, the consequence of a general blood infection."

**PATHOLOGY.**—The liver is symmetrically enlarged and may weigh as much as eight pounds; it is, in general, smooth, herein being distinguished from portal cirrhosis; more frequently than in that disease there are evidences of perihepatitis and of adhesions to the diaphragm and surrounding viscera. This perihepatitis at times gives a very hard surface to the organ. In the latter stages of the disease, where the condition has been of long continuance, as Goluboff pointed out, there may be a certain amount of contraction of the enlarged organ, and the surface may take on a slightly granular appearance. On section, the organ cuts very firmly, and has an intensely jaundiced, dark-green appearance; the gall-bladder is full of bile of good color, clearly indicating that there is no absolute obstruction to the flow of bile from the organ, while the extrahepatic bile-ducts are free from obstruction.

Microscopically, the appearance is characteristic. Frequently, though not always, there can be made out around the larger bile-ducts, which are very

prominent, a more or less concentric overgrowth of new, fibrous tissue, and this fibrosis, instead of being sharply defined toward the lobules of the organ, invades them, passing between the cells; so that there is developed a pericellular condition. With this the fibrosis is very general, so that not only do we have large bands inclosing several lobules, but in addition each individual lobule tends to be surrounded, and, more than that, bands of the new tissue may actually cut off portions of lobules; there is thus developed a unilobular cirrhosis, as contrasted with the multilobular appearance in portal cirrhosis. Another very characteristic feature of the condition is the appearance of the new, fibrous tissue; this tends to be more transparent than, and not so dense as, that seen in the ordinary portal form. Flexner found less elastic tissue developed in this form than in ordinary portal cirrhosis. The new connective tissue is permeated by great numbers of pseudo-bile-ducts.

Nature and distribution of the new tissue in cirrhosis of the liver: 1. In all forms of cirrhosis the white fibrous tissue is increased. 2. Along with the increase of white fibrous tissue there is a new formation of elastic tissue. This new elastic tissue is derived from pre-existing tissue in the adventitia of blood-vessels and the hepatic capsules. 3. Both white fibrous tissue and elastic tissue, in all forms of cirrhosis, may penetrate into the lobules. This penetration takes place along the line of capillary walls or follows the architecture of the reticulum. The chief distinctions between the histology of atrophic and hypertrophic cirrhosis depend upon the degree of extralobular growth and the freedom with which the lobules are invaded. In hypertrophic cirrhosis there would appear to be less interlobular growth and an earlier and finer intralobular growth. 4. The

alterations in the reticulum, *per se*, consist, as far as can be made out at present, of hypertrophy rather than hyperplasia of the fibers. It is still uncertain whether any of the differential methods now in use suffice to distinguish between the reticulum and certain fibers derived from the white fibrous tissue of the periphery of the lobules. Simon Flexner (Univ. Med. Mag., Nov., 1900).

As to the nature of the pseudo-bile-ducts, opinion is divided, some holding them to be of the nature of new formation from the pre-existing bile-ducts, others holding them to represent a late stage in the atrophy of the liver-cells. My own observations lead me strongly to support the latter view, for, in several sections in which they have been abundant, I have clearly made out the transition from the liver-cell to bile-duct.

From comparative anatomic grounds this would seem to be the most reasonable explanation of their development. That is to say, that following the successive stages of the evolution of the liver we find that in its earliest form the organ consists of a mass of independent finger-like follicles. Later these become joined together into a more solid mass, and with this a distinction can be made out between the lower duct-like portions and the secretory terminations of the follicles. Later again the cells become arranged more in reference to the blood-vascular system than to their primary connection as members of separate follicles. But, still, in the human liver the bile-capillaries must be regarded as the representatives of the lumina of separate hepatic follicles, and in peripheral atrophy of the lobules, where that atrophy is not extreme, the appearance which these sections present to me leads me to conclude that the secreting cells

of the liver undergo what I have elsewhere termed "reversionary degeneration." The nuclei proliferate, and in place of obscurely arranged masses of typical liver-cells we obtain small rows of cells resembling those of the bile-ducts, with which they become continuous.

There have of late years been several careful studies of these pseudo-bile-canalculi ("pseudo" because, while suggesting small bile-ducts, in examinations with a high power it is seen that the cells have not the regular arrangement and relationship of those of bile-ducts proper, and there is an absence of a proper lumen).

[Of these studies mention may be made more particularly of those of W. MacCallum (Johns Hopkins Hosp. Rep., vol. x, 1902, p. 375) and Muir (Jour. of Pathol., vol. xii, 1908, p. 287). These bear out the experimental observations of Ponfick, von Weisster, and others. Undoubtedly following upon acute yellow atrophy the new canaliculi are derived by a process of budding and outgrowth from pre-existing bile-ducts, and MacCallum lays emphasis on this process, but, as Muir points out, the bile-duct structures in cirrhosis must be regarded as due both to bile-duct proliferation and to atrophic changes in the liver-cells at the periphery of the affected lobules. A. O. J. Kelly, in his excellent article in the fifth volume of Osler's "Modern Medicine," expresses similar views. J. GEORGE ADAMI.]

Opie in his studies upon chloroform necrosis shows clearly that these apparent bile-ducts can originate from the liver-cells. He finds them, in the regeneration that follows the central necrosis, produced in the central zone of the lobules that is at a distance from pre-existing bile-ducts.

The general appearance of the larger bile-ducts, their abundant and proliferating epithelium, supports the view of Goluboff and some of the recent French

observers, that we are here essentially dealing with a chronic diffuse catarrhal angiocholitis with chronic diffuse peri-angiocholitis. At the same time it may be that the liver-cells are also directly affected, and that there is here a replacement fibrosis in addition to the inflammatory, for the character of the new connective tissue, especially at the margins of and invading the lobules, is not of the productive inflammatory type; there is a lack of small-celled infiltration.

With regard to the other organs, the spleen, as already noted, is, in general, enlarged, and sometimes there is great enlargement. The lymph-glands are not found markedly enlarged, save often at the hilus of the liver; the kidneys and other organs of the body are bile-stained, but beyond that present nothing characteristic.

**PROGNOSIS.**—A few cases have been recorded in which death has been of an acute course, occurring within a month. In one case recorded by d'Espine, in an infant, death occurred on the twenty-fifth day. In general, the disease is of many years' duration.

**TREATMENT.**—The reader is referred to the end of this article, p. 448.

### III. OBSTRUCTIVE CIRRHOSIS.

**DEFINITION.**—The cirrhosis of obstruction of the large bile-ducts.

Two subgroups of this form are recognized, the congenital and the acquired, and regarding the etiology of both there has been considerable debate.

The *locus classicus* regarding the congenital form is J. Thomson's monograph ("Congenital Obliteration of Bile-ducts," Edinburgh, 1892). Altogether

some 70 cases were collected. This form is somewhat more frequent in the male than in the female sex; is characterized by complete obliteration of the common duct in some part of its course, most frequently at the duodenal end; by progressive and extreme jaundice, cholemia, and liability to hemorrhages; by marked enlargement of the liver, with cirrhosis, and by death usually before the sixth month. What is remarkable is the persistence of life under these conditions. Thomson at first regarded the condition as due to a congenital narrowing of the larger ducts, predisposing to catarrh and eventual obliteration. Later in an article in *Allbutt's system* he has put forward the view that the primary disturbance is a descending cholangitis induced by the excretion through the liver of toxic substances circulating in the blood, and this view is actively supported by Rolleston, who brings forward a considerable body of evidence in its favor. He admits that in one case (that of D. Ross, *Lancet*, 1901, vol. i, p. 152) the common duct obliteration was clearly the older process, but quotes from Thomson 7 cases in which a similar progressive jaundice fatal within 17 days was found associated with pervious ducts, and suggests that these represent an earlier stage of the same condition. The fact that the jaundice may be present at birth, or, again, may only show itself some two or three weeks after birth, is also in favor of this view. Rolleston supposes that the condition originates by the passage into the fetal blood of toxic substances derived from the mother, and that these set up a mixed cholangitis and cirrhosis, the cholangitis descending to the extra-hepatic bile-ducts and then causing obliteration. This view is certainly plausible; but, on the other hand, cases are

on record in which with a similar cirrhosis and jaundice there is not only obliteration, but absence, of the common bile-duct. Here there can be question of a descending cholangitis, and, as in Ross's case, already quoted, obstruction is obviously the primary event. It may reasonably be urged that if this can be demonstrated in the one series of cases obstruction may be accepted as an adequate cause of the cirrhosis in the other, without calling in a primary hepatocholangitis. By this I do not mean that cholangitis plays no part in the production of this form of cirrhosis, only that the obstruction is the primary cause.

It deserves notice that the cirrhosis in this series of cases varies from the slighter condition in which the fibrosis is confined to the immediate neighborhood of the dilated bile-ducts up to an extreme grade of monolobular cirrhosis, the individual lobules being completely surrounded by well-developed fibrous tissue. The organ is, in general, enlarged. So also a marked enlargement of the spleen is a common feature.

Lavenson (*Jour. Med. Research*, xviii, 1908, p. 61), the latest writer upon this subject, brings forward further evidence tending in the same direction. He inquires why, if Hanot's biliary cirrhosis is also regarded as a cholangitis, obstruction is not also encountered there, and brings forward embryological evidence to show that an important group of these cases must be regarded as the result of a congenital atresia of the common bile-ducts. While the bile-duct and liver originate as an outgrowth from the small intestine, for a definite period during development they become detached and only later is there secondary junction between bile-duct and duodenal papilla. Imperfect



fusion is well calculated to explain the more frequent obliteration at the duodenal end.

The **acquired obstructive biliary cirrhosis** has, on this continent, been studied more particularly by W. W. Ford (*Amer. Jour. of Med. Sci.*, cxxi, 1900, p. 60), the fullest previous paper being that by Mangelsdorf (*Deutsch. Arch. f. klin. Med.*, xxxi, 1882, p. 522). Something over 200 cases are on record, so that, while advanced cases are uncommon, they cannot be regarded as rare; experience in Montreal shows that moderate grades are much more frequent than the writings of Osler, Sharkey, and Hale White would suggest.

**SYMPTOMS.**—They are those of obstruction—progressive and intense jaundice with cholemia. The feces are colorless, although, where the obstruction is due to a stone, with progressive dilatation of the duct, the bile may eventually escape around the stone and the stools once more become colored. The liver may be enlarged, especially in the early stages, but often—and in the later stages—it is reduced in size. This, together with, in general, no marked enlargement of the spleen and the progressive nature of the icterus, serves to distinguish this form from the biliary cirrhosis of Hanot's type to be presently described. In 10 of Ford's cases ascites and other signs of portal cirrhosis were present. Microscopically, in the slighter cases, as pointed out by Ford, the fibrosis is characteristically confined to the immediate neighborhood of the large bile-ducts, which show some dilatation, and, characteristically also, in the zone of fibrous tissue there is to be observed a wreath-like arrangement of pseudo-bile-ducts. In more advanced cases the disposition

of the new tissue is a mixed type; the organ may be hobnailed; in place of islands of fibrous tissue about the bile-ducts there may be bands with irregular extension of the fibrosis into the lobules. The mixed nature of this more advanced stage would seem to explain the eventual development of symptoms resembling those of portal cirrhosis.

**ETIOLOGY.**—The obstruction is most commonly brought about by the lodgment of gall-stones in the common duct, but cases are on record in which new growths within the duct, cancer of the ampulla of Vater, and of the head of the pancreas, inflammatory stenosis, and in the presence of cicatricial bands tumors and enlarged glands have induced the condition.

There is still debate as to whether obliteration of the common duct in itself without the co-operation of an infective cholangitis will induce this form of cirrhosis. Undoubtedly the commoner sequence of events in obstruction is not cirrhosis, but presumed dilatation of the large bile-ducts and even of the bile-capillaries, and with this as the condition progresses there may also be extensive necrosis of the liver-cells. The difficulty is to harmonize this more frequent sequela with the alternative development of cirrhosis.

The long series of experiments upon ligation of either the common bile-duct or one of its branches in the lower animals beginning with those of Meyer, in 1872, and Charcot and Gombault, in 1876, have given varying results. The majority of observers, it may be laid down, have obtained more or less cirrhosis; but some, like Steinhans and Josselin de Jogn, have only seen cirrhosis when there were signs of coincident infection, while it has been noted that the dog affords less cirrhosis than

the cat and smaller animals of the laboratory. Thus there are the two opposing views:—

(1) That originally enunciated by Charcot and Gombault that the irritation set up by diffusion of biliary products out of the obstructed and distended bile-ducts is the essential cause of fibrosis, and (2) that this alone is inadequate, infection and microbic agents being the true cause. The upholders of the latter view regard aseptic obstruction as leading merely to dilatation and cell necrosis. Without entering fully into the debate, it may be said (1) that in other organs, like the pancreas, without evidence of infection we may obtain either cystic dilatation of the duct or a surrounding fibrosis as the result of ligation of the duct; (2) that, while obstruction by gall-stones more commonly induces dilatation than fibrosis, nevertheless, in both cases, in order to produce the ordinary mixed gall-stone, we now know that bacterial infection of the biliary passage must be present, or, otherwise, it is probable that some infection of the passage exists with both conditions. It is not infection or its absence that is the factor causing the differences; (3) as I have pointed out in connection with the arteries, according to the reactive powers of the individual in one case is developed diffuse arterial dilatation, in another a compensatory fibrosis of the intima and adventitia. Whether cystic dilatation or fibrosis results in connection with biliary obstruction would seem best to be explained as due to the distention, in the one case inducing an *overstrain* of the passages, dilatation and atrophy of the surrounding cells, in the other inducing strain hypertrophy of the surrounding connective-tissue elements, with resulting fibrosis. The irritation, in other words,

in this second case may be sufficient to destroy the more delicate liver-cells, while stimulating the lowlier connective-tissue cells to increased growth. In support of this view is the observed fact that in infants and young individuals fibroid overgrowth (cirrhosis) is the common process, in elderly people dilatation. It is well recognized that in the young the regenerative and reactive tissue growth is greater than in the elderly.

**TREATMENT.** — This will be found at the end of this article, p. 448.

### INFANTILE CIRRHOSIS OF THE BENGALESE.

Here, in passing, reference must be made to what is very possibly a manifestation of this type of disease in the young, to which attention was first called by Gibbons (Sci. Mem. by Med. Off. of Army of India, 6, 1891). Since then several other papers have appeared on the subject. It shows itself in the neighborhood of Calcutta and first in infants about the eighth month, leading to death before the end of the second year. A series of children in the same family is apt to be affected. Syphilis may be excluded; the mother's diet, rich in black pepper and spices, is impugned with resulting faulty digestion on the part of the infants. Gibbons and others describe the microscopical picture of the liver as of the biliary type with perilobular and pericellular fibrosis.

We had in Calcutta in 1907 no less than 636 deaths of children from this disease. Of this number, 92 only were under 12 months of age; 138 only were over 2 years of age. The great bulk of the cases—viz., 64 per cent.—died at ages between 1 and 2 years. The mortality among Hindu children is much greater than among Mohammedans, but male and female children are about equally attacked.

It is important, in connection with the theory that this disease is brought about by absorption of toxic material from the bowels, to note that diarrheal diseases (more particularly acute and chronic enteritis and the complaint corresponding to summer diarrhea) are less common in Calcutta than in England, the mortality from diarrheal disease being 21 per 1000 births in Calcutta, as against 31 per 1000 births in England and Wales (1904). Considering that the disease occurs in sucklings, in infants artificially fed, and in children between 1 and 2 years of age who are given all sorts of food, it is difficult to ascribe the disease to errors of diet. It is generally considered to be a progressive disease and, once started, it is almost always fatal. Taking all things into consideration, we can most reasonably conclude that it is a parasitic disease, but whether microbic in origin or due to larger forms there is no evidence to show. T. F. Pearce (Lancet, Jan. 16, 1909).

### PERICELLULAR CIRRHOSIS.

As already stated, the condition of pericellular cirrhosis exists to some extent in biliary cirrhosis, and in the so-called mixed type of portal cirrhosis a certain amount of pericellular or monolobular deposit of connective tissue is to be recognized. But there exist cases in which the pericellular change is microscopically the most marked alteration in the organ, and, inasmuch as these cases are, in general, unaccompanied by either jaundice or ascites, it becomes necessary to treat them as a separate class.

We rarely, in the adult, meet with a generalized form of the disease. The most frequent examples are to be met with in the infant in connection with congenital syphilis. Not infrequently it is to be found well marked in children born prematurely, whether alive or dead, close upon term. It may, how-

ever, become evident during the first months of extra-uterine life, and where this is the case it often indicates a syphilitic intoxication so severe as to lead to death before the end of six months; rarely do the children survive if the hepatic enlargement is very extensive. Occasionally, however, there may be this diffuse pericellular cirrhosis in the adult, possibly, according to some writers, of the nature of a delayed hereditary syphilis, in which case it is associated with the presence of gummata; in other cases too, more rarely, it is a manifestation of acquired tertiary syphilis. I have seen one case of this in which, in addition to the presence of numerous well-marked gummata, there was this general pericellular development of delicate connective tissue with signs of progressive atrophy of the liver-cells. In this case, however, while the process was diffuse, it was most advanced in the neighborhood of the gummata, and there were areas in the liver showing relatively little fibroid change. Very rarely in tuberculosis there may be a similar pericellular change, though not so extensive as in syphilis.

[In cattle, as first pointed out by Wyatt Johnston (Transactions of the American Veterinary Association, 1893, and Appendix to Report of the Minister of Agriculture for the Dominion of Canada, 1893), there exists in a strictly limited region of Nova Scotia, around Pictou, a disease among cattle characterized by very extensive cirrhosis. The disease appears to be chronic, and death occurs after a brief period of acute delirium or from a progressive paresis passing on to complete paralysis with stupor. The disease most often is first recognized by the acrid taste and odor of the milk, which rapidly diminishes in amount, and with this, or earlier, the coat becomes "staring," the eyes prominent and very bright, and there is considerable looseness of the bowels. There is no jaundice and but a slight accumulation of

fluid in the abdominal cavity toward the later stages. Upon killing the animal the main pathological change is, in general, a moderate enlargement of the liver with some obtuseness of the angles; the surface is perfectly smooth. Microscopically there is marked evidence of parenchymatous and fatty degeneration of the cells, great diminution in their number, and replacement by a delicate and very transparent connective tissue, which in more advanced cases is to be found more dense and more concentrated around the intrahepatic bile-ducts. There is no jaundice; indeed, in the twenty or so autopsies which were performed in this disease the gall-bladder was, in general, very full of bile of light color, the feces were well stained, and, if anything, there appeared to be an excessive excretion from the organ.

Other well-marked features are the presence of a clear, limpid fluid in the abdomen (though this ascites is never excessive), a moderate enlargement of the abdominal lymphatic glands and of the glands at the hilus of the liver, and a peculiar gelatinous edema of the coats of the fourth stomach and small intestines and of the mesenteries. In the fourth stomach, also, there are numerous follicular ulcers, generally found in a cicatrized condition. To the observations of Gilruth, Pethick, and myself upon the causation of this type, I have already called attention.

In some isolated regions in Germany and Switzerland the horses are said to suffer from a similar enzoötic cirrhosis. J. GEORGE ADAMI.]

#### ANATOMICAL CHANGES.—

Leaving aside these cases of pericellular cirrhosis of the lower animals, and referring more especially to the liver of congenital syphilis in the infant, the organ here is found very greatly enlarged, so that in some cases its edge may reach to the iliac crest; the surface is smooth and of a deep-red color, though I have come across cases in which there was a coarsely mottled appearance of relatively large areas of bright-yellow color standing out against the red. Upon section the organ is fairly firm, and, microscopically, the

main feature is this infiltration, between the hepatic cells, of delicate connective tissue with, however, a fair infiltration of small, round cells, the hepatic cells showing evidences of marked atrophy. The portal sheaths are also greatly enlarged, and present considerable infiltration with small, round cells. There are, in general, evidences of the existence of miliary gummata, as minute small collections of round cells not very sharply defined are scattered irregularly through the organ; only in rare cases has the presence of occasional caseous gummata been noted.

According to Hochsinger, four distinct main anatomical changes can be made out: 1. Diffuse small-celled infiltration. 2. Connective-tissue hyperplasia. 3. Miliary gummata. 4. Very rarely true nodular gummata.

Taking all these cases together, it is evident that this condition is distinctly of infectious origin, due, perhaps, not so much to the direct proliferation of the bacteria, for where that is the case, as in tuberculosis and syphilis, there is accumulation of small, round cells at the various foci of proliferation, but due to a toxic effect of the microbes upon the liver-cells, the development of the fibrous tissue being secondary to the atrophy of the parenchyma.

Experimentally, according to Aufrecht, a somewhat similar interstitial or pericellular cirrhosis is producible by the action of small doses of phosphorus frequently repeated. Such minute doses do not, like larger ones, lead to complete necrosis of the liver-cells, but the protoplasm becomes paler, the nuclei more evident and closer together, and the cirrhosis is diffuse and interstitial, exclusively due to the diseased hepatic cells, more especially at the periphery of the acini. As is to be expected, poisons

introduced into the system from without act like those developed within the organism (using this term in its broadest sense), so that some act primarily upon the intestinal walls and only secondarily upon the liver; others act directly upon the hepatic parenchyma, while all vary in their action according to their concentration.

**SYMPTOMS.**—There seem no recognizable symptoms of this condition, *i.e.*, syphilitic pericellular cirrhosis, beyond the extreme enlargement of the liver, which is tender, and the coexistence of other evidences of the disease. There is, as above said, no ascites and no jaundice.

As above stated, this variety of cirrhosis frequently leads to intra-uterine death and to premature birth, and, where the child survives birth, death, in general, occurs before the sixth month. Upon examination, using Levaditi's or other appropriate stain, abundant spirochetes may be encountered throughout the liver-tissue, more particularly in the livers of cases of syphilitic abortion or death shortly after birth. Where the enlargement of the liver is extensive, there appears to be little chance of recovery, though mercurial treatment has resulted in some recoveries.

Hochsinger found that of 148 infants with congenital syphilis 46 showed clinical enlargement of the liver. The large number of 30 of these are stated to have recovered. Five cases came to autopsy, and in one the enlargement was due to tuberculosis. In none of his cases was there icterus or jaundice; in these enlarged livers there was some extent of fat infiltration. He is strongly in favor of immediate mercurial treatment.

**MALARIAL CIRRHOSIS.**—In this relationship may be noticed the rare

development of a definite grade of cirrhosis in severe cases of malaria, noted years ago by Kelsch and Kiener, and seen in tropical and subtropical rather than in the temperate zones. The liver is large and at most finely granular. There is the further resemblance to infective biliary cirrhosis in the huge size of the spleen. Certain French writers have also described a *tuberculous* cirrhosis, which, again, comes into this category.

Cirrhosis of the liver, due to chronic malarial poisoning, is not of infrequent occurrence in Bombay, and that, too, in young children, where all the possible contributory causes except malaria can be eliminated. Besides the liver, the stomach, spleen, and kidneys are severely affected. There is a history of ill health and enlargement of the spleen for some years, with repeated attacks of intermittent fever. The enlargement of the spleen becomes marked, and there is a profound secondary anemia. Later there is great emaciation and distention of the abdomen from collection of fluid in the peritoneal cavity. The fluid is not very abundant as a rule, and in many cases it does not recur after tapping. After weeks of treatment with iron, quinine, and arsenic the patient may improve greatly, and the spleen diminish in size. In the last stages there is profound debility and emaciation, with the late toxic symptoms seen in other forms of cirrhosis. On opening the abdomen the most prominent object is the enormous spleen. The capsule is thickened and often adherent to one of the neighboring organs. The liver is somewhat small, but not as much so as in alcoholic cirrhosis. The red corpuscles may be reduced to 1,500,000 to the cubic millimeter. The malarial parasite present in the peripheral blood is usually the benign tertian. To sum up, therefore, we have in malarial cirrhosis a complex condition, of which the hepatic dis-

case is the terminal event. Ascites is late. The finely granular surface of the liver is quite distinct from hob-nail liver. The cirrhosis results from repeated attacks of malarial hepatitis and capsulitis, associated with perisplenitis and a plastic peritonitis. The adhesions resulting from the latter, along with the dragging of the enlarged spleen, produce extreme deformities of the stomach. Plastic peritonitis varies in amount, but is always a feature in the case. Tucker (*Lancet*, May 23, 1908).

The cases of cirrhosis of the liver and ascites in children, met with so often in the tropics, are the outcome of a chronic malarial poisoning. The disease is a slow fibrosis, starting in the liver and spleen, and finally ending in interstitial nephritis. It is the result of repeated attacks of malaria, especially when neglected, upon young, unresisting, and possibly badly fed subjects. Duprey (*Lancet*, Aug. 1, 1908).

**ARTERIAL CIRRHOSIS.**—Contrary to what I believe is the generally received opinion, I find that in cases of general arteriosclerosis branches of the hepatic arteries resemble other arteries throughout the body in showing a distinct periarteritis. Hasenfeld has noted similarly a slight chronic endarteritis in the hepatic arteries in arteriosclerosis.

This periarteritis is rarely extreme and clinically is incapable of recognition, though Eichhorst is inclined to recognize a senile variety of cirrhosis due thereto, and analogous to the arteriosclerotic nephritis resulting from arteritis and periarteritis in the renal vessels.

This arterial change is only of interest in that a large proportion of subjects with alcoholic cirrhosis present also a condition of general arteriosclerosis, and thus associated with alcoholic cirrhosis there may be independently a

certain amount of fibroid development in the portal sheaths due to the arterial disturbance. With Rolleston I fully agree that for practical purposes such arterial cirrhosis is negligible.

Certain writers have suggested that the toxic substance leading to the development of what I have termed "portal cirrhosis" is brought to the organ by the arterial branches; if this be so, the anatomical evidence of the transmission is singularly small.

**CENTRIOLOBULAR CIRRHOSIS.**—In cases of well-marked obstructive diseases, either of the heart or of the lungs, the liver is the seat of great, passive congestion, with atrophy of the central cells of the lobule. There is no sign of fibroid development in these regions; all that is to be seen is the great dilatation of the central capillaries of the lobule, with atrophy of the cells. In cases of a more chronic type with less severe obstructive disease we occasionally meet with a well-marked development of fibrous tissue immediately round the central vein of the lobule. It is debatable whether this is of the nature of a replacement fibrosis in consequence of the atrophy of the central liver-cells or whether it may be termed "non-functional" or "non-inflammatory," due to the increased pressure in the hepatic veins and the altered character of the blood-flow. This form, again, while it may be predicated in cases of long-continued slight mitral or other obstructive disease, is associated with no clinical symptoms.

Hanot and Gilbert have, however, described a venous "hypertrophic" liver with enlargement, the organ remaining enlarged. If this form truly exists, it will be clinically impossible to differentiate it from the enlargement due to accompanying passive congestion.

**SECONDARY CIRRHOSIS.**

**SYNONYMS.**—Cirrhosis following upon perihepatitis; Glissonian cirrhosis; *zuckerguss leber*; multiple hyaloseritis.

As emphasized at the beginning of this article, it makes for clearness to separate sharply the condition of chronic progressive perihepatitis or hyaloseritis from the cirrhoses. There is here no true cirrhosis, no diffuse laying down of fibrous tissue, within the organ. The condition is better considered along with the various forms of peritonitis.

Chronic perihepatitis may either be localized, and in patches over the surface of the liver, or it may also be generalized. Such generalized perihepatitis is a very characteristic condition pathologically, though clinically it may be present in an advanced form without any signs of its presence, and, on the other hand, may appear and be almost, if not quite, indistinguishable from the atrophic and contracted form of portal cirrhosis.

**ETIOLOGY.**—Such thickening of the capsule of the liver may be one of the results of a general peritonitis; indeed, it must be regarded as one evidence of such a condition.

Of 22 cases of universal perihepatitis in the post-mortem records at Guy's Hospital collected by Hale White (Allbutt's "System of Medicine," vol. v, p. 118), in only 2 was it stated there was no peritonitis; in 17 it was distinctly stated to be present, and in the remaining 3 no mention was made of the peritoneum. Hale White suggests that in his cases the peritonitis was always fibroid and so never owed to tubercular growth; this, however, is contrary to the observations of other writers, and I myself have seen a most marked condition of universal perihep-

atitis accompanying and evidently due to a chronic peritoneal tuberculosis, though it is true the thickened capsule in such cases does not show a characteristically tubercular appearance throughout, but is fibroid in its deeper layers and homogeneous. But a study of chronic tuberculous pleurisy shows that the process may assume this homogeneous fibroid character. In fact, it may be said that this form of universal fibrous perihepatitis is distinct from localized chronic perihepatitis in that it is an extension of inflammatory disturbance from without the liver, and not from within, as may often happen in the latter condition, and that anything capable of setting up a chronic productive inflammation in the abdominal cavity is also capable of producing this form of disease.

**PATHOLOGICAL ANATOMY.**

—In consequence of the deposit of this thickened, new, fibrous tissue over the surface of the organ and its contraction, the liver becomes more globular in appearance than normal, though it is to be noticed that, in general, the thickening is more marked on the upper and anterior surface than on the under surface. Frequently, as Fagge, I believe, was the first to point out, the anterior edge is folded over on to the dorsum in a manner that is difficult to explain. Frequently, also, the omentum, shortened and thickened by the universal peritonitis, is adherent to the lower edge of the organ, and this thickened mass may be mistaken for the edge of the liver. Frequently, again, the productive inflammation on the surface leads to adhesions, more especially anteriorly and to the diaphragm.

As Hale White points out, often little pits are to be seen on the surface of the thickened capsule; when seen they

are very striking. I have only seen them upon the upper diaphragmatic aspect of the organ in regions where there have been no adhesions, and from their position and character I am inclined to believe that they are brought about by little eddies opposite to the lymph stigmata in the under surface of the diaphragm. A marked feature is the ease with which the thickened capsule can be peeled off, leaving, in general, a smooth surface.

Authorities differ as to the connection between this perihepatitis and cirrhotic change in the organ itself. According to Murchison and Osler, it is frequent, but Fagge, Hale White, and Curschmann speak of the condition as usually unaccompanied by any interstitial inflammation. And, in the not very frequent cases which I have come across, I also have found the liver soft and pulpy, rather than fibroid. Evidently both conditions may exist, and, speaking correctly, it is only the former condition where there is this extension of the inflammatory process inward along the lymphatics, leading to the development of fibrous bands within the organ, or, again, where there is an extension upward of the process into the organ along the sheaths of the portal vessels at the hilus, which ought properly to be spoken of as cirrhosis.

With regard to other organs. The spleen, in general, shows a like capsular thickening, more especially of its diaphragmatic surface, and, as Hale White, who has made the fullest study of the condition, points out, there is a very frequent complication of interstitial nephritis.

**SYMPTOMS.**—Frequently, as above stated, there are no symptoms recognizable; but, in a typical condition of the disease, we find the liver smaller

than normal, with thickened, uniformly blunt edge, and, associated with this, marked ascites.

Hale White points out that the condition is of long duration, and that the ascitic fluid can be repeatedly tapped. There is an absence of jaundice, while evidences of chronic peritonitis and, again, of interstitial nephritis are well marked.

At times a friction sound can be made out over the liver, though this is rare; more frequently the organ, by adhesions to the abdominal wall, becomes fixed, and it does not move downward on inspiration.

In London apparently this condition is fairly frequent, for Fagge makes the statement that, at Guy's Hospital, for every 5 cases that die showing portal cirrhosis with ascites there is 1 in which the ascites is associated with perihepatitis.

**TREATMENT.**—See below, page 448.

**SPORADIC CIRRHOSIS.**—I would employ the term, "sporadic cirrhosis" to indicate those cases in which there is a fairly extensive development of fibrous tissue throughout the liver in scattered patches related definitely in origin to no one special portion of the lobule or of its surrounding sheath. Where the development is slight, we can scarcely speak of cirrhosis; but in some cases the connective-tissue development may be very extensive, and here we must speak of cirrhosis.

Two main series of cases are to be included under this heading:—

1. The fibrous-tissue development in consequence of the presence of multiple infectious granulomata: a condition seen in tuberculosis and syphilis.

2. The condition to which our attention has been more especially directed



by Welch, Flexner, Barker, and the Johns Hopkins School, in which, apparently from the action of toxins rather than from bacteria, multiple focal necroses are developed in the liver. These focal necroses pass through the successive stages of slow death, infiltration with leucocytes, and organization and formation of fibrous tissue, leading eventually to the development of fibrous tissue; so that scattered through the organ are little, irregular nodules of fibrosis.

Yet a third form may be recognized, for the recognition of which we are again indebted to Welch, namely: that form of cirrhosis due to the conveyance into the liver by lymph or blood of discrete particles of foreign matter, as, for example, of carbon or of stone. Around about such little collections of foreign particles there may be developed here, as in the lung, a noticeable amount of fibrous tissue; but, in general, the condition is very slight.

I have come across it both in connection with anthracosis and again in connection with stonemason's lung, or silicosis; but, to the best of my belief, Welch's well-known case of cirrhosis anthracotica is the only very extensive and truly cirrhotic case upon record.

**1. Cirrhosis Due to Infectious Granulomata.**—In general, tuberculosis affecting the liver leads to no recognizable symptoms, even though the liver be thickly studded throughout with fibroid tubercles; very rarely we have a caseous mass. Beyond, therefore, mentioning the existence of this form, and the previous note upon a rare, more diffuse cirrhotic change described by certain French observers, regarding which there is some little doubt, it is unnecessary for me to say anything further concerning it.

With syphilis it is different. Here dense bands of new tissue may radiate in various directions around the fibroid and caseous gummata. Where these gummata are frequent, the obstructive effect of the bands and again the deformity of the organ may lead to signs and symptoms which closely simulate either the atrophic or parenchymatous hypertrophic form of portal cirrhosis. But even in the most extensive cases the development of this fibrous tissue is so sporadic, and the condition of the other parts of the organ is so relatively healthy, that, strictly speaking, these cases ought not to be spoken of as cirrhotic.

For its symptomatology, this gummatous form depends upon the number and the position of the gummatous growths in the organ and the amount of fibrosis developed in the immediate neighborhood. As these gummata have no points of election and may occur on the upper surface and away from the vessels at the hilus as frequently as they occur in its neighborhood, it follows that we may have, on the one hand, an advanced gummatous condition of the organ unaccompanied by jaundice, or by ascites, or by any recognizable disturbance, while, on the other hand, there may be but a few gummata, and yet these, being situated in such a position as to obstruct either the main branches of the portal vein or some of the main bile-ducts within the organ, may induce either ascites, or icterus, or both. In advanced cirrhosis, where there are numerous gummata, it may be possible to palpate the lower portion of the organ, and to recognize the scarred and coarsely nodular condition of the surface; or, again, as in advanced portal cirrhosis, the organ may be, by the contraction of the fibrous tissue, so retracted behind the

ribs as to be incapable of being felt. Where this is the case, it is impossible to make a diagnosis between tertiary syphilis and the liver of alcoholic cirrhosis, unless the evidence of syphilitic infection of other organs is present. Where there is doubt as to the nature of the condition, progressive improvement manifested under the potassium-iodide treatment will clear up the diagnosis. Osler distinguishes a group of cases in which the patient is anemic, and passes large quantities of pale urine containing albumin and tube-casts; the liver is enlarged and, perhaps, irregular, and the spleen also is enlarged, while ascites may supervene. In such a case the presence of gummata is associated with amyloid degeneration of the organ, of the intestinal mucosa, and of the spleen. He further points out what is, perhaps, not very uncommon: that the large, projecting masses of liver-tissue produced by the contraction of gummata affecting the left lobe are apt to be mistaken for new growths occurring in connection with the organ. Here, again, potassium iodide affords valuable aid in diagnosis.

In brief, the history of syphilitic infection and the effects of treatment by potassium iodide are the main diagnostic aids in differentiating syphilitic or other forms of cirrhosis.

**2. The Cirrhosis of Focal Necroses.**—As yet we know and pathologically have been able to recognize singularly few cases of cirrhosis originating from focal necroses. Such focal necroses occur in a large number of infectious diseases. Not only have they been recognized by Welch and Flexner in diphtheria, by Reed and subsequent observers in typhoid fever, and by numerous observers in tuberculosis, but by Guarnieri, Thayer and Hewetson, Barker, and others in malaria, and

Flexner, in his experimental work upon toxalbumins, has been able to show that several vegetable poisons of the nature of toxalbumins will produce them and follow the development of cirrhosis following upon these focal necroses.

[Hanot (Comptes-rendus de la Soc. de Biol., p. 469, 1893) describes as *taches blanches du foie infectieux* certain appearances which, he points out, characterize the liver in all forms of infectious disease: small, irregular areas of pale color, appearing more especially on the convex surface, in which upon microscopic examination a condition of dilated capillaries with abundant intravascular and extravascular leucocytes are to be made out. The liver-cells in the regions show degenerative changes. The condition is allied to, but not so advanced as, the focal necroses. J. GEORGE ADAMI.]

As to the exact causation of the necroses, some doubt must, I think, still be expressed. While it is possible that, as many observers believe, they are directly due to the action of toxins, it is difficult to comprehend why such toxins should pick out only specially isolated portions of the organ. One would expect to find that in addition to the action of the toxins there is some disturbance of the circulation, some thrombosis or other change in the smaller veins or capillaries of the part whereby the cells, being imperfectly nourished, undergo destruction.

[The above paragraph, written ten years ago in the first edition of this article, is reproduced without alteration, inasmuch as it represents very accurately the continued uncertainty regarding the causation of these focal necroses. The only advance to be chronicled is the increasing evidence in favor of the conclusions reached in the final sentence, namely, the capillary thrombosis plays an active part in many of the cases. Here the work of Pearce and his associates deserves especial notice (Jour. Exp. Med., vol. viii, 1906, 64, and Jour. of Med. Research, vol. xv, 1906, 99). This has shown that the toxins which

are capable of inducing these necroses exert *in vitro* marked hemolytic and agglutinative action; that thus they can be explained by the destruction and conglutination or agglutination of red corpuscles and the products of their disintegration within the hepatic capillaries, leading to the formation of hyaline thrombi. Experimentally it can be seen that such toxins cause necrosis followed by fibrosis.

As bearing upon the production of cirrhosis and what has already been said regarding the succession of stages from acute yellow atrophy up to portal cirrhosis it is worthy of note that extreme cases of puerperal eclampsia induce an extensive necrosis of the liver, very similar to that seen in the first of these conditions, whereas cases in which the action upon the liver is slighter exhibit necrotic areas undistinguishable from the focal necroses seen, for example, in typhoid fever. We appear thus in puerperal eclampsia to obtain a connecting link between these various conditions and an indication that in the ordinary portal form of cirrhosis destruction of the parenchyma cells is an important factor in the overdevelopment of the fibrous tissue; in other words, another indication that the fibrosis, at least in part, is of the replacement type. J. GEORGE ADAMI.]

**TREATMENT.**—The results obtained from medicinal treatment depend entirely upon the stage of development that either of the forms described has reached. When seen early a case may be greatly improved and cured by appropriate dietetic, prophylactic, and medicinal measures; even a well-established case may sometimes be at least held in check by judicious medication; when, however, the hepatic parenchyma has been destroyed and replaced by fibrous tissue, it is obvious that no treatment can restore function and that our only resource is palliation.

When the case is seen early, the measures indicated are those employed in acute hepatic congestion, the object being to reduce, as much

as the general condition of the patient will allow, the work of the liver. For a couple of days a spare **milk diet**, or, better, **milk and Vichy** only, will serve to create a relative ischemia of the diseased organ. If there is pain, **cupping** and even wet cupping over the organ may be necessary. Or, the **ice-bag**, interposing a few layers of gauze between it and the skin, may suffice. A **mustard poultice** or plaster is also useful by diverting blood to the surface. If there is constipation, it is preferable not to give purgatives at first, but to use large lukewarm **enemas**, containing a tablespoonful or two of glycerin.

As to internal medication intestinal sepsis must be as much as possible encouraged. The best agents for this purpose are **sodium benzoate**, **salol**, and **sodium salicylate**, giving 5 grains (0.3 Gm.) of either with a full glass of water four times a day.

After the hepatic congestion has been relieved, the dietetic measures to be adopted are those indicated in any stage of cirrhosis and in any of the forms described. Alcoholic beverages, even beer, tea, coffee, and condiments, all of which tend to enhance hepatic congestion, should be avoided; meat and eggs are the most fertile sources of liver poisons our ordinary food contains; fats, when the liver is torpid and fails to secrete bile, are not sufficiently saponified and emulsified; they undergo decomposition in the intestine, form irritating acids, which in turn irritate the liver, thus forming a sort of vicious circle.

The chief articles of food indicated are: vegetables of all kinds and fruit; milk, preferably buttermilk; cereals and starches, with a moderate

use of sugars. Fish, with the exception of the oily varieties, such as shad and salmon, are usually well tolerated; oysters likewise. Grapes, carefully avoiding the skins and seeds, have been found so useful in cases of hepatic hyperemia tending toward cirrhosis that in Europe **grape cures** (2 to 12 pounds being consumed twice daily) have been in vogue many years. **Buttermilk "cures"** also exist, 3 to 4 large glasses being taken twenty minutes apart three times daily. As beverage, alkaline mineral waters, especially **Vichy** (source, Célestin), should be given preference.

The early symptoms of cirrhosis demand treatment for the gastric catarrh and intestinal subinflammatory conditions. **Tartrate of sodium** in effervescence is useful for this, with a few minims of **dilute hydrocyanic acid** in each dose, given every six hours. Milk and arrowroot, or yolk of egg and milk, is an appropriate diet. Whey, or curds and whey, and koumiss are useful. A **mustard cataplasm** to the epigastrium is helpful, if there is a tendency to esophagismus or vomiting. **Bromide of ammonium** relieves the irritability of the pharynx. When the digestive powers return, the best treatment for the liver consists in full doses of **ammonium chloride** and **fluidextract of taraxacum**, sweetened with liquid extract of licorice; this should be maintained for some weeks. If the digestive powers are weak, **sodium bicarbonate** with **gentian**, **rhubarb**, **tincture of capsicum**, and some **nuxvomica** will prove of advantage. All strong liquors should be forbidden. The patient should be duly informed as to the nature of his ailment, and made to understand the risks of continuance in the use of spirits and other vicious habits. **Inunction with biniodide of mercury ointment** may be carried out from time to time over the hepatic region. Sir Dyce Duckworth (Practitioner, Nov., 1912).

Four cases described by the writer were apparently cured by a limited **milk diet** (6 glasses), medical treatment, including administration of **hexamethylenamine**, and insurance of regular bowel movements, all alcohol being forbidden. After improvement, the milk was increased to 8 glassfuls, and later fruit allowed. Milk or almost exclusive milk diet was continued for at least 2 months, and followed by light diet of simple foods. N. S. Davis, Jr. (Jour. Amer. Med. Assoc., July 26, 1913).

Saline purgatives are useful to insure free action of the bowels and deplete the portal system. A small dose of **sodium sulphate**, 1 or 2 teaspoonfuls in a glass of hot water each morning, or a glassful of **Carlsbad water**, or **Hunyadi** twice a week or oftener if needed; or, again, 2 teaspoonfuls of effervescent magnesium sulphate, also in hot water, every other day, serve a good purpose. **Warm baths**, followed by **friction** with a rough towel over the region of the liver, serve to prevent frequent recurrence of hepatic congestion. **Cold compresses**, i.e., a towel wrung out of cold water applied over the organ and covered with a piece of flannel, night and morning, is said to increase the flow of bile.

When the stools indicate by their color a deficiency of bile, **oxgall**—the *fel bovis purificatum*—in 5-grain (0.3 Gm.) doses, also in capsules, is sometimes very efficacious. **Hepatic opotherapy**, giving preferably **calf or pork liver**,  $\frac{1}{4}$  pound slightly cooked, or, better, carefully hashed and given in bouillon or soup, is often helpful. If the patient tires, or cannot take the dose by the mouth,  $\frac{1}{2}$  pound of pork liver is macerated in a pint of cold water and given by rectal injection,

after an enema, to clear the intestine. Hepatic opotherapy is always more efficacious when given with a **pure milk diet**. (See also article on Animal Extracts: Hepatic Organotherapy.)

Personal, but advanced, case in which the beneficial effects of **hepatic organotherapy** lasted but ten days. Up to 1905, 25 cases had been reported in which hepatic organotherapy has been used. There were 12 cures; 7 of these were in cases of atrophic cirrhosis, 4 of hypertrophic cirrhosis with ascites, and 1 in which the volume of the liver was not indicated. In 6 of these cases the satisfactory condition of the patient was established thirty-six days, three months, five months, eight months, one year, and two years after discharge. In the latter, recurrence manifested itself by oliguria six months after the hepatic opotherapy had been stopped. Resumption of the pork liver soon restored health. E. Gyr (*Revue méd. de la Suisse Romande*, June 20, 1908).

The writer employed **hepatic organotherapy** in the case of a woman in which, besides atrophic cirrhosis and splenomegaly, there were indications of hepatic insufficiency, *e.g.*, torpor, hypothermia, etc., and ascites. She improved rapidly; the splenomegaly and ascites disappeared. Oulmont (*Société Méd. des Hôpitaux*, May 29, 1908).

Case of cirrhosis in a woman of 46 years treated with fresh **pork liver**, 125 Gm. (4 ounces) daily; **calomel**, and a **milk diet**. All the symptoms improved promptly, particularly the ascites. The writer believes that benefit would only be temporary, alimentary glycosuria having proven positive, thus denoting insufficiency of the hepatic cell. Galliard (*Revue de therap.*, Oct. 15, 1908).

The influence on oliguria is a good index of the efficiency of **hepatic organotherapy** in cirrhosis. If the volume of urine passed daily is not reduced, the hepatic lesions may be deemed too far advanced to be influenced by this method. Perrin (*Paris méd.*, Dec. 16, 1911).

The writer recommends a **milk diet** in the early stages of cirrhosis of liver. This leaves the organ comparatively in repose while promoting diuresis. He gives nothing but water the first day and a purge. An adult should take 3 liters of milk during the day, sipping a small amount every 1 or 2 hours, to avoid distending the stomach, thus causing retention and fermentation and injury to the liver cells. The milk must never be taken raw, but goat's or asses' milk may be substituted for cow's milk. Fermented milk or condensed milk, etc., should not be used except when the patient wearies of the sterilized milk. This milk diet should be kept up for a month. After this the ordinary diet can be very slowly and gradually resumed, keeping to small meals of easily digestible foods. Terol (*Revista Ibero-Amer. de Ciencias*, July, 1918).

In fully developed cirrhosis in any of its forms the treatment is essentially the same. In certain cases the business connections of the patient, especially brewers, barkeepers, liquor dealers, etc., oblige them to imbibe more or less freely. The substitution of hard apple or pear cider for all drinks in such cases transforms their business necessities, as stated by H. C. Wood, Sr., into a continuous treatment. **Buttermilk** is also useful in this connection.

Recently, **keratin** has been recommended, particularly in the treatment of chronic cases.

The writer, who first used keratin in hepatic cirrhosis, recently observed a case in which caffeine and calomel had failed to stay the disease. The **keratin** treatment, continued over a year, caused the organ, at first enormously enlarged, to recede to normal. The author then tried it in a case of Laennec's cirrhosis. The primary dosage was small—five 0.5 Gm. (7½ grains)

tablets daily—because of the accompanying gastroenteric congestion. **Bismuth** was used as a corrigent and the dose of keratin slowly increased. **Caffein** was also used steadily, along with the X-rays over the liver. After 5 months of this treatment, during which 3 paracenteses were necessary, no more ascites formed and all edema disappeared, with simultaneous diuresis. Danilowsky (Berl. klin. Woch., Feb. 23, 1914).

The writer regards **keratin** of more value in the treatment of cirrhosis of the liver than the iodides. Owing to the chronicity of the complaint, it is especially valuable, owing to the fact that it has very few if any untoward effects. S. M. Zypkin (Berl. klin. Woch., Feb. 23, 1914).

**Arsenic** is a drug of considerable value in cirrhosis of the liver. The employment of mild purgatives, **charcoal and magnesia**, for securing intestinal antiseptics, is of great importance. When intestinal fermentation is well marked he advises cautious administration of **naphthol** or **salicylic acid**. All alcoholic beverages should be interdicted. Foods that do not produce toxic material—eggs, fruit, vegetables, baked meats—are recommended. Small quantities at frequent intervals are preferable to large amounts taken at long intervals.

**Caffeine** and **theobromine** act as direct excitants of the renal parenchyma. In contrast with the saline diuretics, which appear chiefly to provoke elimination of water and at the same time of salts, and especially chlorides, the xanthin bodies increase the elimination of nitrogenous elements, and especially urea and uric acid. Anten (Arch. inter. de pharm. et de therap., vol. viii, fasc. v and vi, 1901).

Report of a case which improved remarkably under the administration of **apocynum cannabinum** (Canadian

hemp), 5 drops (0.3 c.c.) of the fluid-extract thrice daily. Whenever the patient interrupts it for a few days ascites reappears. F. J. Bowles (Therap. Gaz., Feb., 1901).

The writer advises the following: Attention to gastrointestinal digestion, because if the food supply of the organism is perverted or reduced it cannot be expected to recuperate. The elimination of bile from the liver should be increased by the administration of **sodium glycocholate** with the addition of small doses of **mercury**. The fluidity of the bile can be increased by the administration of **alkaline mineral waters** with **sodium salicylate**. **Biniiodide of mercury** with **iodide of potassium** has a very beneficial effect in many cases of nephritis which are associated with hepatic insufficiency. Hepatic cirrhosis is the result of a toxemia and its treatment must, therefore, consist in the removal of the cause of the intoxication, with, at the same time, stimulation of the liver, so that it may do its part in the oxidation and elimination of the poisonous substances. Richardson (Med. Rec., Oct. 8, 1904).

Courtois-Suffit recently (Bull. de la Soc. Méd. des Hôp., Jan. 24, 1919) observed 4 cases showing that a possible syphilitic origin should be suspected, until disproved, in every case of cirrhosis of the liver, both ascites and alcoholism present. EDITORS.

The writers recommend a strict milk diet in alcoholic cirrhosis of the liver. Eight ounces are given every two hours. The second month soup is added to the diet. **Calomel** and **sulphate of soda** are administered, the first being given in  $\frac{1}{4}$ - to  $\frac{1}{2}$ - grain (0.021 to 0.032 Gm.) doses every morning for a week, to be followed the next week by 80 grains (5.3 Gm.) of **sulphate of magnesia** each morning, the two remedies being alternated. **Hot affusions over the liver** are made every morning, and at night a **cold compress** is applied. If there is no albuminuria a **blister** 4 by 2 inches is applied **over the liver** every tenth day. Daily **massage of the abdomen**

is employed. If the case progresses favorably the diet can be varied, but the calomel and sulphate of magnesia should be continued. **Iodide of potassium** should not be given except in syphilitic cases. The best means of noting the progress of the case is to have the patient weighed every day, the weight being an indication of the progress of the ascites. If the fluid increases, the patient should be **tapped**. Huchard and Fiessinger (Jour. des praticiens, June and July, 1905).

The writer recommends an absolute milk regimen in the beginning of the treatment. Later a mixed diet may be allowed—eggs, potato purée, peas, beans, rice, tapioca, etc. In patients with nypopepsia, kefir or other kinds of fermented milk may be added. **Saline purgatives** in small doses are to be recommended. **Calomel** is of value and **sodium salicylate** advisable. Among the recommended formulas are:—

℞ *Sodii benzoatis* . gr. lxxv (2.5 Gm.).

*Strychnina sul-*

*phatis* ..... gr. ss (0.03 Gm.).

*Aqua dest.* ..... ℥x (300 c.c.).

Two drams (8 Gm.) daily.

℞ *Sodii benzoatis* .. gr. v (0.32 Gm.).

*Sodii phosphatis* . gr. x (0.65 Gm.).

In cachets; 2 cachets to be taken after meals.

If the ascites is marked, the author prescribes an absolute milk diet, drastic purgatives, **scammony** associated with **squill** and **digitalis** or with **theobromine**. M. Gaston Lyon (Jour. de méd. de Paris, No. 47, 1906).

The writer recommends for treatment a diet somewhat mixed, finely divided in form, fluid, or brothy, with little fat, well cooked and as free as possible from spices, such as pepper. No salad or vegetables prepared with fat, and generally no raw fruit, are allowed. Lean meat thoroughly cooked, in bad cases cut fine or shaved, may be given in small quantities. Alcoholic beverages should be denied as a rule, but when the patient

cannot be deprived of them without loss of appetite light beers or wines may be given in small, accurately prescribed quantities. A true disinfection of the intestine cannot be made, but the bowels should be kept open with **purgatives** or **mineral waters**. In the later stages, characterized by stasis in the region of the portal vein, ascites, dilatation of the collateral veins, formation of varices on the gastric and hemorrhoidal veins, and edema of the lower extremities, more energetic treatment is necessary. The ascites may be relieved by **puncture**; **diuretics** are to be given; the condition of the heart and kidneys is to be observed and regulated. **Mercurial preparations** have been recommended many times as remedies in cirrhosis of the liver, but aside from the cleansing of the bowel by **calomel** these preparations are chiefly beneficial when the cirrhosis is due to syphilis, and they should be pushed whenever there is suspicion of a syphilitic origin. Hoppe-Seyler (Med. Klinik, June 13, 1909).

Careful differentiation is of paramount importance in the treatment. In all stages dietetic treatment and regulation of the bowels are the principal thing. Milk should be the main feature of the diet, sweet, sour, or buttermilk, watching over the urine, especially the excretion of urobilin. **Saline laxatives** for a time may be needed, a warm solution of **Carlsbad salts** in the morning or **cascara** at night. In the early stages it is often an easy matter to restore conditions to normal in this way, especially when the trouble is due to abuse of alcohol. Organs are able to recuperate amazingly, and particularly the liver, if it is not being constantly subjected to new injury. If the liver is enlarged and hard, with more or less tendency to jaundice, the spleen somewhat enlarged, and the abdomen distended, the wearing of an abdominal band may be useful to keep the overheavy organs from sagging or being pushed about, thus interfering still further with the portal circu-

lation. The binder should not be allowed to interfere with the movements of the diaphragm. With ascites, the writer warns not to wait too long before **tapping**; release of the fluid restores better conditions for the circulation. Drugs which act on a weakened but still sound heart or on the kidneys or render the blood more fluid may sometimes cure the tendency to ascites with cirrhosis of the liver. Even salt, which aggravates dropsy with kidney or heart disease, may draw the water out of the tissues and expel it through the kidneys. The writer cites Savy's case to illustrate this: A man of 51 with atrophic cirrhosis of the liver had required tapping six times in two months, each time over 12 liters (quarts) of fluid being withdrawn. He was kept on a milk and salt-free diet, but, wearying of this, he cast aside all restrictions and ate at will, using salt lavishly, up to 25 or 30 Gm. ( $6\frac{1}{4}$  or 8 drams) a day. By the end of a few weeks the ascites had disappeared, and has not returned. C. Bäumlcr (Deut. med. Woch., Feb. 8, 1912).

Gastric hemorrhage, with or without hematemesis, is frequently encountered in cases of cirrhosis. It is met with especially in the precirrhotic stage of Laennec's cirrhosis, becomes infrequent in the stage of ascites, and shows increased frequency again in the cachectic stage of the disease. In the prophylaxis of these hemorrhages, sudden changes of blood-pressure in the portal system must be carefully avoided. To this end a **milk diet** should be prescribed, and the milk given only in small, frequently repeated amounts. Exertions as well as all nervous impressions which might react on the abdominal vascular tension, should be prohibited. Systematic **saline purgation** will do good, and the application of **leeches** may at times be availed of in order to reduce arterial tension.

In the event of actual hemorrhage, **ice** should be given internally and **morphine** hypodermically. Hemostatic remedies and vasoconstrictors or coagulants must be resorted to. **Ergotine**, **calcium chloride**, **gelatin** injections, and especially injections of fresh **antidiphtheritic** or other **antitoxic serum**, are measures which may be employed with success.

Three deaths personally known to have followed the operative treatment of hemorrhoids, and, at the necropsy, cirrhosis of the liver was discovered for the first time. In all cases of hemorrhoidal disease a thorough knowledge of the state of the liver should be obtained before any operative interference is advised. In the treatment of ascites mild **purgation** and **calomel** from time to time; **calomel** also used in  $\frac{1}{40}$ -grain (0.0016 Gm.) dose every three hours as a diuretic. The old-fashioned pill, **digitalis**, **squills**, and **calomel** and **copaiba** are useful. **Tapping** is resorted to early and frequently. J. H. Musser (Phila. Med. Jour., June 15, 1901).

The benefit from copious diuresis was illustrated repeatedly in the writer's cases. In an elderly woman one drug after another was tried without effect, including **digitalis**, besides restriction of fluids and warm baths. But striking benefit followed a course of small doses of **calomel**, 25 mg. ( $\frac{1}{2}$  grain) with 400 mg. (6 grains) milk sugar, 3 times a day. The output of urine increased from about 500 c.c. (1 pint) to 3 liters (quarts) a day and then averaged under the **calomel** 1800 c.c. ( $3\frac{1}{2}$  pints). **Echinococcus**, gall-stones or syphilis require special treatment. Van Spanje (Nederl. Tijdsch. v. Genesck., May 4, 1918).

**Saline-solution enteroclysis** is a valuable agent at almost any stage. It enhances diuresis where this is necessary to reduce ascites. The rectal use of antiseptics such as **ichthyol**, **potassium permanganate**,



**boric acid**, etc., has been advocated; but the large doses required do not speak in favor of this method, as toxics in general tend to activate the morbid process in the liver, owing to its function as a detoxicatory organ. They should, therefore, be used sparingly.

**Ascites.**—When ascites appears, **potassium** or **sodium iodide** in small doses is said to be useful; 3 grains (0.2 Gm.) may be given four times daily in a glassful of water. **Arsenic** has also been advocated: 3 drops (0.18 c.c.) of **Fowler's solution** after meals. The kidneys must also be kept active. The most normal of diuretics is urea in 20- to 30- grain (1.3 to 2 Gm.) doses, but the infusion of **digitalis**, freshly made, 1 to 2 teaspoonfuls three times daily, or **potassium acetate**, 30 grains (2 Gm.) every morning, or **theobromine**, 5 grains (0.3 Gm.) three times daily, unless the gastric disorder be marked, are generally preferred. A tea of **buchu** and **uva ursi** leaves, each 2 drams (8 Gm.) in 1 pint (500 c.c.) of water, is very useful. This should be taken warm in three doses daily. It makes a pleasant beverage and acts gently though efficaciously upon the kidneys. The bowels should also be kept active, preferably by **saline purgatives**, the drastic purgatives serving only to aggravate the trouble. Diaphoretics and even Turkish and Russian baths are advocated by some.

When, notwithstanding our efforts, the ascites increases, **paracentesis abdominis** is necessary. It is best not to wait too long. It is an easy procedure which affords the patient marked relief. This and the other surgical measures indicated at this stage are enumerated and ably com-

mented upon by B. M. Ricketts (New York State Medical Journal, Sept. 18, 1909) under the following fourteen headings:—

"1. **Incision through abdominal wall**; *a*, temporary drainage; *b*, permanent drainage. A number of patients have been treated in this way with most gratifying results. A few have recovered permanently, while others have been greatly benefited. Why this should be from simple incision with immediate subsequent closure is not understood. Among the most interesting cases of recovery is that reported by Clay, 1907, who reports one of cirrhosis of the liver cured as the result of an operation for the relief of strangulated umbilical hernia.

"2. **Puncture through abdominal wall**; *a*, temporary drainage; *b*, permanent drainage. Paracentesis abdominalis has been done for centuries for the removal of fluids of any character or to relieve distention, and its effects upon an enlarged liver no doubt observed, but it did not become a routine curative measure until late in the last century. McSwiney, 1865, drained the peritoneal cavity twice, to alleviate the urgent symptoms, due to cirrhosis of the liver. Aron, 1868, did it repeatedly, in a given case, for the same condition, due to thrombosis of the vena porta, in which there was persistent biliary secretion. Wilson, 1879 (Youngstown, Ohio), contributes an interesting report, of frequent paracentesis, for cirrhosis of the liver. Courtenay, 1881, records one in the tropics in which recovery resulted from paracentesis three times performed. Duncan, 1881; Armangue, 1881, and Flint, 1883, each speak of the value of repeated paracentesis.

Lithgow, 1882, gives one of the first recorded cases of recovery resulting from paracentesis abdominis (twelve times) for cirrhosis of the liver. Macdonald, 1889, reports a recovery resulting from repeated aspirations. Donate, 1885, reports a case in which he made paracentesis sixty-six times. Gravirowski, 1891, ably discussed the influence of paracentesis abdominis in atrophied cirrhosis of the liver on assimilation of fats from food and nitrogenous metabolism. Portes, 1898, in dealing with alcoholic cirrhosis made thirty punctures, removing 234 liters of fluid. Lecreux, 1902, with sixty-five punctures, removed 1750 liters of fluid.

**"3. Hepatotomy (knife);** *a*, temporary; *b*, permanent. Incising the liver at various depths after having first opened the abdomen is of recent date. It has been done for both temporary and permanent drainage with more or less benefit. Whether the benefit results from hepatotomy alone or the combined influence of peritoneal irritation resulting from incising it, or the manipulation of the viscera necessary to incise the liver or venous anastomosis resulting from the inevitable hepatopexy to follow the repair of the liver and abdominal incision, has not been determined. Each has an important influence, and when all are combined that influence must be more beneficial.

**"4. Hepatotomy (trocar);** *a*, temporary drainage; *b*, permanent drainage. Harley was an advocate of the free use of a large-sized trocar in many acute and chronic diseases of the liver, among them cirrhosis. An occasional report of this having been done has appeared. The trocar may be used with or without an incision,

and the results are similar to hepatotomy with knife for the same reasons. Hornibrooke, 1886, punctured the liver for hepatitis.

**"5. Cholangiostomy.** Knowsley Thornton, 1887, described a method of draining the biliary tract by which he penetrated the right lobe to the gall-bladder if open; if not, to the hepatic duct. This is a most desirable way to do it, especially when the lobe is much enlarged. Also in the event of the common duct only being occluded and the bladder contracted upon itself, this method may result in perfect drainage of the biliary tract. (Ricketts, Transactions of the New York State Medical Association, 1889, No. 12, page 895.) Cut through the lobe of the liver and pull the gall-bladder (when large enough) through the lobe as far as possible; anchor it so that it will become united to the liver-tissue. When this is done, open the bladder at a subsequent time; drain externally. This is a modified cholangiostomy.

**"6. Cholecystenterostomy.** This consists in uniting the gall-bladder to the large or small gut that drainage might be more perfected. This has been done by Combemale and Dubar, 1900. It is indeed the exception that this is done with better knowledge, because of the dangers of infection from the alimentary tract.

**"7. Cholecystotomy.** The operation is a rational one when the common duct is occluded from any cause, but irrational when the hepatic or cystic duct is closed, or the gall-bladder contracted upon itself. Bernard, 1901, drained the biliary tract in this way for cirrhosis of the liver. C. T. Souther, 1906, resorted to this method with fatal results."

In biliary cirrhosis drainage of the bile-ducts by **cholecystotomy** is a proper operation after systematic treatment has failed. In 105 patients with cirrhosis and ascites 42 per cent. were improved and 50 per cent. were not improved; the mortality in thirty days was 29.5 per cent. There was nothing peculiar in the 9 cases in which permanent relief occurred; when the omentum was sutured between the layers of the abdominal walls, the mortality was slightly less and the percentage of improvement slightly greater. Drainage apparently increased the danger of the operation. When adhesions or perihepatitis existed the prognosis was better. The dangers of the operation were mainly due to the condition of the patient rather than to the procedure. Therefore, the selection of suitable cases demands great judgment. It is of no use in ascites due to other causes than cirrhosis of the liver, and is contraindicated in the presence of renal or cardiac disease. Nevertheless, it has proved of benefit in a certain number of cases of cirrhosis, primarily for the relief of the ascites and secondarily for the relief of other symptoms of portal congestion. Greenough (Amer. Jour. Med. Sci., Dec., 1902).

An exhaustive study of the biliary cirrhosis and their surgical treatment has led to the following conclusions: The best method of treating biliary cirrhoses of the liver surgically is by means of **cholecystostomy**. This operation can be used in all the forms of biliary cirrhosis, inasmuch as it removes the biliary stasis and diminishes the congestion of the liver. The operation is especially indicated in the hypertrophic form of biliary cirrhosis, with chronic jaundice, known as "Hanot's type." When the lesion of the biliary system is associated with an obstructive endophlebitis in the portal system in the liver, and, when as a result there is an increased tension in this system of veins so that an effusion of fluid takes place into the abdominal cavity, the treat-

ment must, in addition, embrace the relief of the ascites. This may be done by operation (see below), in addition to the drainage of the gall-bladder mentioned above. Cignozzi (Riforma Medica, Dec. 23, 1905).

"8. **Injection of Caustics.** This has occasionally been resorted to upon the theory that the irritation which they produce would aid materially in increasing the activity of the peritoneum. Among the more common agents employed for this purpose are alcohol and the iodine preparations injected, both crystals and solution into the liver and upon its peritoneal covering. Beerens, 1896, to determine the effects of Vienna paste upon a cirrhotic liver, applied it to this organ after having first performed paracentesis abdominalis."

[These procedures are of historical interest only, and should not be resorted to. Ed.]

"9. **Ligation of Vena Cava and Vena Portæ.** Occluding these vessels by ligature has been done several times to divert the venous flow from the liver, but the results have not been altogether satisfactory. It is probably not so good as other less serious methods for the relief of cirrhosis of the liver. Pascale, 1901, described surgical intervention in cirrhosis of the liver by 'catura della vena cava e della vena porta.'

"10. **Hepatopexia.** This operation consists in suturing the liver to the anterior belly wall so that it may become firmly fixed to it. This was accomplished by Delagènière, 1897, in a case in which he also did a cholecystostomy.

"11. **Omentopexy.** This is accomplished by implanting the omentum into the tissue of the abdominal wall or upon the peritoneum overlying the

anterior belly wall. It is also described as epiplopepy, omentofixation, and venous anastomosis, and is done with suture or other means of fixation. It is described as the **Talma**, **Talma-Drummond**, and **Morrison** methods, and has given results for the cure and relief from symptoms far superior to any yet devised. **Talma**, 1889, began the first rational work for the relief of liver cirrhosis, but it was not until 1892 that von Lens (a student of **Talma**) reported the results of **Memlen's** operation, that the advantages of omentofixation were made known. In 1896, **Drummond** and **Morrison** reported the first cure due to omentofixation and drainage of the peritoneal cavity. **McArthur**, 1901, and **Hurtado**, 1902, implanted the great omentum (**Morrison**) into the abdominal muscles for cirrhosis of the liver. **Weber**, 1899, mentions a case in which the symptoms of hepatic cirrhosis were arrested by peritoneal adhesions. **Morrison**, 1899, cured by operation a case of ascites due to liver cirrhosis. **Frazier**, 1900, and **Clementi**, 1900, each record successful results by operations for liver cirrhosis. **Roe**, 1901, accomplished this with dissolution eight months later, at which time verifying, by autopsy, its effect upon the abdominal viscera (there was present a horse-shoe kidney). And **Landerer**, 1902, did one by the **Talma-Drummond** method. **Zuccaro**, 1901; **Gardini**, 1901; **Lastari**, 1900; **Annovazzi**, 1901; **Ballin**, 1901; **White** (2 cases), 1903, and **Shaw**, 1903, each report successful results from surgical operations. **Keen**, 1903, records a case of cirrhosis of the liver with ascites, subsidence of ascites six months after the operation, and non-recurrence in two years.

**Herczel**, 1902, operated (**Talma**) for liver cirrhosis; patient observed well one and three-quarter years after. **Grosz**, 1903, succeeded in curing a case of cirrhosis of the liver, while **Levai**, 1904, did so in 2 cases, and **Bindi**, 1905, 1 case by **Talma's** method. **Wheeter**, 1905, by combining the **Talma** and **Morrison** methods, succeeded in curing a case of liver cirrhosis. **Monroe** and **McGregor**, 1906, cured a case of cirrhosis of liver by epiplopepy, and **Ketchem** and **Thomson** succeeded in doing so by omentopexy."

Case successfully treated by **Talma's** operation. The statistics of the procedure seem to indicate a mortality of from 40 to 60 per cent., while an almost certain fatal result attends medical treatment. **Smith** and **Carson** (*Interstate Med. Jour.*, June, 1906).

If **Talma's** operation is not more frequently carried out, the reason may partly at least be found in the high mortality immediately following the operation or within the next two months.

The statistics of the **Talma-Morrison** operation and its modifications and substitutes are unfavorable partly because many patients have been operated on too late to do good, and when the risk of failure was excessively great on account of other organic disease. Such a thing happens in all new operations, but, instead of stopping operative treatment altogether, it should, if the operation has a single feature in its favor, lead only to more careful selection, earlier diagnosis, and greater care in the operation and after-treatment. Moreover, the death rate and the shortening of life must not be compared with similar incidents in persons previously healthy, or persons with trivial diseases. As in so many other border-line diseases, we should think chiefly of the pain and disability, and the inevitable death within a relatively short time, under the usual methods

of treatment. From that standpoint, a single patient made comfortable for a time beyond the usual expectation outweighs many others whose days may have been lessened, though they lost nothing they ever could have gained in function. In such a case it seems only fair to put the matter as plainly as possible before the patient, and to let him decide. Many, in the case reported, will prefer the cathartic and the trocar, just as many others will refuse to stop the injurious habits against which they are warned. Some, however, will prefer a definite risk with the hope of relief, and it is in order to show what may be done even under many disadvantages that the writer has brought up the subject at this time.

From every point of view it is desirable to operate early, before the liver has undergone advanced degeneration, and before toxemia and disease of other organs have made the operation too dangerous. George Dock (*Jour. Amer. Med. Assoc.*, Jan. 22, 1910).

Ascites is not always due to disturbances in the portal circulation, but is more liable to be the expression of chronic peritonitis. This theory throws a light on the infectious and toxic factors in the origin of cirrhosis, and it also suggests that the **Talma operation of omentofixation** is not applicable in every case. The very fact that the ascites was cured immediately by this operation in a number of cases showed that the cure could not have been due to establishment of a collateral circulation, as this requires time to develop. The writer knows of over 300 cases in which the Talma operation has been employed, but permanent benefit was obtained in only 30 per cent. of the 274 cases compiled by Bunge. It is adapted only for the cases in which the portal circulation is actually the causal factor. Klopstock (*Berl. klin. Woch.*, Jan. 30, 1911).

Through the use of **omentopexy**, even in the condition of advanced hepatic degeneration and general tox-

emia, with resulting ascites, over 10 per cent. of symptomatic cures are obtained, and over 50 per cent. at least are improved, comforted, and given increased lease of life. As this advanced condition is often preceded by a period of latency (a year or more), during which pathognomonic symptoms develop, early diagnosis of this mortal lesion justifies exploration and repair, with improved prognosis. The surgeon should not be deterred from making an exploratory operation for diagnostic purposes, as all forms of cirrhosis are fatal when treated by the expectant methods. H. H. Grant (*Interstate Med. Jour.*, June, 1912).

In ascites secondary to vascular cirrhosis of the liver, the contraindications to surgical treatment are: organic disease of the heart or lungs and Bright's disease; age beyond 55 or 60; marked jaundice; emaciation, or hebetude.

The writer administers morphine and atropine half an hour before the operation, which he performs in the following manner: The peritoneum is exposed through a 4- or 5- inch median incision after the integument has been injected with a 0.1 per cent. solution of cocaine or novocaine. The posterior sheath of the right rectus is incised longitudinally near the inner border of the muscle and the latter separated gently from the posterior sheath. The procedure is repeated on the left side, after which the muscles are retracted and a transverse incision made through the peritoneum, care being taken not to cut the vessels in the round ligament. After having determined the condition of the viscera, the omentum is drawn through the incision and held upward by an assistant while the lower lip of the incision is sutured to the posterior surface of the omentum, care being taken to prevent wounding or including large vessels. The omentum is then drawn downward and tucked behind the recti muscles and round ligament. Several catgut ligatures are necessary to re-

tain the omentum in its new location. The upper lip of the incision is sutured to the omentum and the abdomen is closed in the usual manner. In debilitated patients the linea alba should be overlapped.

The most important advantages are as follows:—

1. Possibility of thorough inspection of the abdominal viscera.

2. Utilization of practically the entire surface of the omentum without disturbing the normal relation of the stomach and transverse colon.

3. Prevention of compression of the omentum between the muscle and its sheath.

4. Practical elimination of danger of postoperative hernia and intestinal obstruction.

5. Avoidance of injury to blood- and nerve- supply of the recti muscles. E. A. Babler (*Jour. Amer. Med. Assoc.*, April 13, 1912).

Referring to **Talma's operation** or **omentopexy**, the writer states that statistics show that while the percentage of operative deaths is steadily diminishing, the ratio of cures remains about the same, viz.,  $\frac{1}{3}$ . An additional  $\frac{1}{6}$  shows improvement, however, so that about  $\frac{1}{2}$  of all the patients operated upon are benefited. Cases of hypertrophic cirrhosis are more favorable than those of the atrophic variety. Again recovery results only some time after the operation in some instances; thus in a case reported by Pal and Frank, cure followed only 18 months later. The results of surgical treatment seem fairly encouraging. Juilliard (*Revue Med. de la Suisse Romande*, Feb., 1913).

A study of 212 cases published by 42 different operators showed that **Talma-Morison operation** for Laennec's cirrhosis offers better prospect for success when the patients are in the thirties, instead of in the fifties, although successful cases are known in patients of 60 or more. The cases in which syphilis is responsible for the cirrhosis give by far the best prognosis in all cases of ascites, provided the syphilis is treated.

The cases of cirrhosis of the liver with ascites fall into two great classes; those in which the ascites is the result of progressing obstruction of the portal system by the encroaching cirrhosis—a purely local trouble, and those cases in which the portal system is not much obstructed but the weakness of the heart action entails the ascites. In the first group, omentopexy to aid in development of collaterals offers great chances for relief and an approximate clinical cure. Without some such intervention the patient is doomed. In the other group, the immediate prognosis is less grave, and omentopexy will have little influence on the course of the case. It should be considered only as the very last resort in this group, after failure of treatment of the heart disease and possible syphilis. Simon (*Nordiskt Med. Arkiv.*, Oct., 1917).

In a study of spontaneous and operative cure of cirrhosis, describing 3 cases, the writer concludes that cure by the **Talma operation** cannot be due only to the establishment of adequate circulation. The liver and probably the spleen must undergo a change. He deems the spleen involved by cirrhosis to a greater degree than is generally believed. Riesman (*Jour. Amer. Med. Assoc.*, lxxvi, 288, 1921).

**"12. Eck's Fistula.** This is accomplished by dividing the vena porta, ligating the central end and implanting the peripheral end into the vena cava, by lateral anastomosis. A patient operated upon by Vidal by this method lived four months. Hematemesis did not return, but ascites returned six weeks before death.

**"13. Splenopexy.** The spleen may be anchored to the anterior peritoneal wall independently, or together with an omentopexy, or hepatopexy, with most gratifying results, both as to

partial and complete cures. Among those who have done this, Norath reports 1, Frank 2, and Koch 1 case."

**Splenectomy**, according to the writers, is indicated not only in Banti's disease, but also in Hanot's cirrhosis of the liver and in hemolytic icterus. The writers describe a case of successful splenectomy for cirrhosis of the liver in a child of 8. The icterus disappeared eight days after the operation and the enlarged liver decreased markedly in size. The patient returned home so that the case was not followed any further. Eppinger has recently collected the cases in which splenectomy has been performed for hypertrophic cirrhosis of the liver, and they show that the operation is justified. A histological picture of the spleen in these cases is given, showing a marked increase in connective tissue. The changes are similar to those in Banti's disease, which shows many points of similarity to cirrhosis of the liver; the similar results of splenectomy also indicate a relationship. But of course the two conditions are not identical, there being many points of difference in their symptomatology and course, but it seems certain that the spleen plays a part in the pathogenesis of both.

They further describe two cases in which splenectomy was performed for hemolytic icterus. This disease may be acquired in very early youth. Banti performed splenectomy in hemolytic icterus with success; since then it has been successfully performed by numerous surgeons. It is most successful in the familial form, but Micheli has reported good results in acquired hemolytic icterus. The two cases reported by the authors were the acquired form. The icterus disappeared soon after the operation and did not return. Anemia was no longer perceptible, and the results of splenectomy have caused many authors to believe that the spleen plays the chief part in the

pathogenesis of hemolytic icterus. Others have pointed out that the early improvement does not persist, so that there must be a primary change in the red cells or defective function of the bone-marrow; but Eppinger holds that a supernumerary spleen of lymph-glands may enlarge and assume the pathological function of the spleen.

Sometimes adhesions form after the operation that result in serious consequences for the patient. In the second case described they finally caused death. This must be taken into consideration in deciding the indications for the operation. Nobel and Steinbach (*Surg., Gynec. and Obstet.*, from *Zeitsch. f. Kinderh.*, xii, 76, 1914).

**Splenectomy** and similar procedures afford a ready means of reducing the portal circulation for the purpose of relieving the subnormal liver of its overload. Mayo (*Annals of Surg.*, Aug., 1918).

"14. **Multiple Visceroplexy**. The possibilities of hepatospleno-omentoplexy might well be considered. This may be accomplished at one or multiple sittings, preferably one, the primary operation. The result of either could better be accomplished by all. As a greater volume of blood could thereby be diverted with no additional risk, and without impairing the function of either."

Additional data upon the medical and surgical treatment of ascites are given under **ASCITES**, in the second volume.

J. GEORGE ADAMI,  
Montreal.

**CITRATE OF MAGNESIUM.**  
See **MAGNESIUM**.

**CITRIN OINTMENT.** See **MERCURY**.

**CLEFT PALATE.** See **SURGICAL ANAPLASTY OR PLASTIC SURGERY**.

**CLIMATIC BUBO.**—This disease was described by Ruge in 1896. It consists of a non-venereal bubo or adenitis, which occurs in tropical countries, the East Coast of Africa, the West Indies, China, etc., both epidemically and endemically. Individuals who live under similar hygienic conditions, sailors and soldiers, for instance, seem predisposed to it.

**SYMPTOMS.**—The disease usually begins with a swelling in the inguinal region of either one or both sides, accompanied by fever of a remittent type. The bubo or buboes gradually enlarge until they attain the size of a hen's egg or more, then gradually subside after several weeks or months. The swelling being inflammatory, the neighboring tissues become involved and suppurate, leaving fistulous tracts, which heal with difficulty. The gland is painless and the duration of the disease is prolonged—conditions which do not prevail in bubonic plague, from which it is to be differentiated.

**PATHOGENESIS.**—It has been considered by some observers as a mild form of bubonic plague due to some kindred pathogenic organism conveyed by some insect. But it affords none of the dangers of this disease, and is comparatively benign. The bacteriology of the disorder is still unknown, though staphylococci are present when suppuration occurs. Malaria, at one time deemed an etiological factor, is now disregarded as such.

The disease is probably parasitic. The writers found refringent elements containing chromatin cells resembling broken-down phagocytes in the capillaries and cells of typical cases. Letulle and Nattan-Larrier (Bull. de la Soc. de Pathol. Exotique, Dec. 14, 1910).

**TREATMENT.**—As soon as the inflamed glands tend to suppurate they should be freely incised and the contents carefully washed out with antiseptic solutions. The methods indicated for warm abscess (see Abscess, Volume I), including lead lotion and an ichthyol and belladonna ointment, are as applicable here. Rest is an important feature of the treatment. The biniodide of mercury in  $\frac{1}{16}$ -

grain (0.004 Gm.) doses, three times daily, or potassium iodide, 5 grains (0.3 Gm.) with equal frequency, tends to promote recovery whether a history of syphilis can be obtained or not. Quinine is also helpful. S.

**CLIMATOLOGY.** See MINERAL SPRINGS AND CLIMATOLOGY.

**CLOVES.**—Cloves are the unexpanded flower-buds of *Caryophyllus aromaticus*, an evergreen of the East and West Indies, having a deep-brown color, highly fragrant odor, and a hot, acrid taste. They contain a volatile oil, 18 per cent. (*oleum caryophylli*), which is a pale-yellow fluid when freshly prepared, becoming dark brown in color later on. In addition to this, cloves contain *eugenin*, a tasteless, crystalline substance; salicylic acid, and *caryophyllin*, a neutral, tasteless, odorless body.

*Eugenol*, U. S. P., or eugenic acid, is an aromatic liquid, soluble in alcohol, but slightly so in water.

**PREPARATIONS AND DOSE.**—The only official preparation is the oil, *oleum caryophylli*, the dose of which is 1 to 5 minims (0.06 to 0.3 c.c.).

The British Pharmacopœia has an official infusion, *infusum caryophylli*, the dose of which is 1 to 2 fluidounces (30 to 60 c.c.).

**PHYSIOLOGICAL ACTION.**—These preparations act as an aromatic stimulant, antispasmodic, antiseptic, anesthetic, carminative, and counterirritant. They are stimulating and tonic to the stomach and intestines.

In overdose the oil acts as a soporific, produces violent gastroenteritis, and kills by causing respiratory failure. It is eliminated by the skin, kidneys, liver, and bronchial mucous membrane.

**THERAPEUTICS.**—On account of its stimulating and tonic action on the intestines cloves may be given to prevent griping in *diarrhea*. The oil may be used locally in *muscular rheumatism*, and relieves the pain in *toothache* by destroying the sensation of the nerve. In combination with lanolin it is said to be of value in *eczema*, and separates the epithelium in *lupus vulgaris*. The oil is a parasiticide



and is frequently used in **pediculosis pubis**, and is said to retard the growth of the tubercle bacillus in peripheral **tuberculosis**. Eugenol is an antiseptic and anesthetic, and is used in dental and minor surgery. H.

**CLUB-FOOT.** See ORTHOPEDIC SURGERY.

**CLUB-HAND.** See ORTHOPEDIC SURGERY.

**COAGULATION TIME OF THE BLOOD.**—Coagulation is the normal property of the blood when it is outside of the vessels. In the white corpuscles there is a zymogen known as prothrombase, which becomes thrombase through the action of the calcium salts. The blood also contains a proteid known as fibrinogen. When the blood is shed, thrombase acts upon the fibrinogen, producing fibrin. The fibrin is an insoluble substance and causes the blood to coagulate. The time necessary for this coagulation to occur depends upon many conditions.

A knowledge of the coagulating time of the blood is useful and of value in many disorders and intoxications.

Normally the blood coagulates in from two to eight minutes, but this time is influenced by various factors, among which may be mentioned atmospheric humidity, ingestion of certain drugs, the part of the body from which the blood is taken, the time of the day, and the time in reference to the patient's last meal.

The coagulation time is found to be hastened by a temperature exceeding that of the body, contact with foreign matter, any injury to the walls of the blood-vessels, agitation, and the addition of calcium salts. Conversely, it is found to be delayed or prevented by a low temperature, the addition of neutral salts or oxalates, peptones, and contact with oil or living vessel walls.

In taking a specimen of blood the lobe of the ear, the tip of the finger, or, in the case of infants, the great toe may be used. The part should first be thoroughly cleansed with water, followed by alcohol, and then allowed to dry. The puncture is

then made large and deep enough to cause a free and sufficient flow of the blood.

**TESTS.**—A test accurate enough for ordinary purposes and one which can be performed at the bedside is as follows: Several drops of blood are placed on a cleaned glass slide. These drops are tested at regular intervals by drawing a straw or horsehair through them until the fibrin is seen to adhere to it. The difference between the time when the blood was drawn and the formation of the fibrin may be said to be the coagulation time.

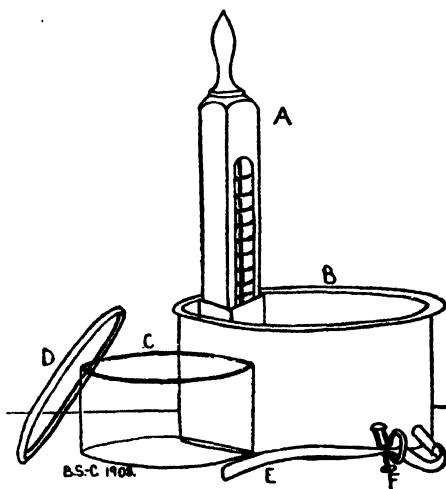
**Milian's Test.**—This method is also imperfect and uncertain, but may be used in a general way. A drop of blood is allowed to fall on a large glass slide, which is gently tilted from side to side at regular intervals. The drop of blood at first is pear-shaped when tilted, but gradually assumes the form of a blunt cone, which denotes the completion of coagulation. The time necessary to produce this is, on an average, five minutes if the blood is normal.

The writer has devised an apparatus based on Milian's method, but which eliminates the errors due to evaporation and temperature change. It consists of a German Stender dish, 80 mm. in diameter and 40 in height; a small pan with an outlet and with a bracket for holding a thermometer (an ordinary tin baking pan, the outlet and bracket being made by a tin-smith, will do), a bath thermometer, a wide elastic band, a piece of rubber tubing, a stop-cock, and a millimeter scale. The rubber tubing is attached to the outlet of the pan and clamped with a stop-cock, and the thermometer slipped into the bracket or holder. The pan is filled with water at 37° C. (98° F.) and maintained there by the addition of hot or cold water as required. The Stender dish is cleansed, the rim smeared with lanolin or petrolatum, the lid thoroughly cleansed and applied, and held in place by the rubber band. The dish is then placed, everted, in the pan of water. The ear or finger is next thoroughly cleansed and given a free puncture with a clean, sharp instrument, so that the blood flows

freely without undue pressure. The Stender dish is removed from the water, quickly dried, and the elastic band removed. The first drop of blood is wiped off and note is made of the time the second drop appears. This drop, while on the finger or ear, is lightly touched to the upper surface of the inverted lid of the Stender dish held horizontally. The part is then wiped off and several other drops are similarly deposited on the lid on either side of the median line, the time of the appearance of each drop being also noted. The dish is then placed on the lid and the rubber band applied. Placing the millimeter scale under the inverted dish, the size of the different drops is quickly measured and noted. Only those drops are regarded whose diameter measures 5 or 6 mm. The dish is then placed back in the water bath with the lid underneath. At intervals the dish is removed from the water and held vertically, while the contour of the drops is rapidly observed from the side or the density studied by looking at the drops through the lid. As quickly as possible the dish is returned to the horizontal position and replaced in the water. So long as, when observed from the side, the drops sag, are tear-shaped or pear-shaped, or, when looked at full, are denser below and clearer above, coagulation has not occurred. As soon as the drop is rounded on profile view, and of the same density throughout when seen from the front, coagulation is completed. To confirm this, the dish is removed from the lid and the clot is picked off with a needle or straw. The time at which coagulation was first observed is noted, and the period between this and the moment the drop appeared on the part is taken as the clotting time. With this method results are surprisingly constant. Solis-Cohen (Univ. of Penna. Med. Bull., Aug., 1908).

**Modification of Milian's method.** The instrument consists simply of a glass slide, on which are mounted

with balsam two glass disks 5 mm. in diameter. In making a determination, the surface from which the blood is to be obtained is anointed with a thin layer of petrolatum, the first drop of blood wiped away, and the surfaces of the glass disks touched to the next drops in such a way that each disk is completely covered with blood. Drops of correct depth having been obtained, the slide is inverted over a glass nearly filled with water at a temperature of 40° C. (104° F.) and covered with a



Myer-Solis-Cohen's apparatus. *A*, ordinary bath thermometer; *B*, zinc pan (common tin pan will answer); *C*, German Stender dish; *D*, lid of German Stender dish; *E*, rubber tube; *F*, clamp.

sponge or folded cloth wet with water at the same temperature. After five minutes the slide is removed at intervals of one minute, held vertically in front of a white surface, and the surface contour of the drops of blood noted. So long as the blood is fluid the drops hang down; but after coagulation has proceeded to a certain degree the drops fail to change in shape when the slide is tilted, maintaining a spherical contour. This is taken as the end-point. It appears sharply and is easy to determine. The coagulation time as determined by this method varies in normal cases from six to nine

minutes; abnormally, it may be as great as forty minutes. The chief source of error lies in the using of drops of incorrect depth. Gross errors in this respect do not, however, come practically into consideration, and, as a rule, several drops, as ordinarily picked up, clot within two minutes of each other. Duke (Archives of Internal Med., Feb., 1912).

**Wright's Method.**—This is much more accurate, although taking more time and being more complicated. Wright's coagulometer is used. This consists of a copper reservoir in the bottom of which is a rubber mat, while in the side is a small opening, to which is attached a rubber tube having a pinch-cock. A rack holding a thermometer and twelve capillary tubes fits into this reservoir. Each tube is numbered, the number corresponding to that beside each small opening in the rack. Each tube is about 10 cm. in length, having a lumen the diameter of which is about 0.25 mm., and marked at 5 cm. from its lower end. A rubber cap also fits over the blunt end. The reservoir is about half-filled with water, which is then heated to 37° C. (98.6° F.—blood heat) or 18.5° C. (65.3° F.—half blood heat), preferably the latter. While the water is being heated the tubes are carefully cleaned with water, alcohol, and ether, and then dried. When the temperature of the water is at the desired point the tubes are placed in the rack with their rubber caps downward, and allowed to remain there until they reach the temperature of the water. They are then removed and dried and the rubber caps are taken off. Having punctured the finger, or lobe of the ear, the blood is drawn up in tube No. 1 to the 5 cm. mark, the time noticed, and the tube placed in the proper opening in the rack, this time with its pointed end downward. At regular intervals of about one minute the blood is drawn into each tube, which is then treated in the same manner as tube No. 1, carefully noting the time each tube is filled. Each tube is then removed at regular intervals, a piece of blotting paper held close to its end, and the blood then tested by blowing through the tube and noting how readily it flows

out. This procedure is gone through until one tube is found in which the blood remains upon blowing into it. The difference between the time the blood was drawn into this tube and the time when it could not be expelled is the coagulation time of the blood.

In cleaning the tubes, the clots are dislodged with a fine wire, and the tubes washed in water, alcohol, and then ether.

**Russell and Brodie's Method.**—This test is even more accurate than Wright's, but requires a microscope. The coagulometer used is a small, moist chamber with a glass bottom, which is placed upon the stage of the microscope. Projecting into the moist chamber is a small cone of glass the end of which is about 5 cm. in diameter. A drop of the blood to be tested is put on the end of this cone, which is immediately fastened to the moist chamber, the time being noted. There is another fine tube, which passes through the side of the glass chamber, to the outer end of which is attached a hand bulb, and by this means a gentle stream of air is directed against the drop which is observed through the microscope. At first the corpuscles move freely, but later on they do not move so freely and the drop begins to change shape. The air is forced against the drop at regular intervals, until finally all motion of the corpuscles has ceased, and there is only an elastic motion of the drop, the part of the drop displaced by the force of the air springing back into place as soon as that force is removed. This is considered the terminal point of coagulation.

The Brodie-Russell is more reliable than the Wright instrument. The average coagulation time is between three and six minutes. The proof of a delayed coagulation must be based upon several observations. The coagulation time is not affected by the ordinary changes in room temperature. Blood obtained simultaneously from different points on the surface of the body shows no marked variation in the coagulation time. A delayed coagulation is not constantly associated with jaundice due either to benign or to malignant obstruction. F. T. Murphy and A. H. Gould

(Boston Med. and Surg. Jour., July 14, 1904).

Out of 251 cases tested by Boggs's modification of the Brodie-Russell method, 163 cases have coagulation times below 8 minutes, and, although more than half the series are pathological cases, there are only 88 with times above 8 minutes; 97 had times of 11 minutes or above. The longest time in the series is 33 minutes. Leaving out these 37 cases the remaining 214 cases have an average time of 6 minutes and 40 seconds. Records below 7 to 8 minutes are normal, while coagulation periods passing this period are proportionately delayed. Hinman and Sladen (Bull. of Johns Hopkins Hosp., vol. xviii, Nos. 195 and 196, 1908).

**Lenoble** (Bull. de l'Acad. de méd., Nov. 7, 1916) imprisons a little air in the test tube with the blood (Hayem's hematimeter). On tilting the tube the air moves around, like the drop of fluid in a spirit level, as long as the blood is fluid. The moment the blood begins to coagulate, the bubble of air is immobilized.

The physician should inquire as to the personal and family history in respect to hemophilia and thrombosis, with examination of the skin for traces of extravasation, phlebitis, etc., and test the coagulating time. When the tests show excessive coagulability of the blood, thrombosis menaces, and ether and chloroform should be avoided as they injure the blood and may bring on thrombosis. In such a case blood-serum should never be injected, and it must be remembered that losses of blood enhance the coagulating power of the blood. The blood can be rendered less coagulable by **citric acid**. Chantemesse prescribes it in the daily dose of 12 to 18 Gm. (3 to 4½ drams) diluted in water. **Sodium citrate** might answer the purpose. Subcutaneous injections of **saline** or **glucose isotonic physiologic solution** might be useful, or a 47 per 1000 solution of **sugar** by the drip method. P. E. Weil (Presse méd., Apr. 12, 1917).

**Coagulen** (Kocher-Fonio), according to H. K. Bonn (Jour. Ind. State Med. Assoc., Oct. 15, 1917), consists solely of blood platelets and is rich in thrombokinase, an essential and important part in the mechanism of blood coagulation. For use the coagulen powder is dissolved in sterile normal saline solution boiled for 3 minutes. Fonio states it is never necessary to employ any solution stronger than 5 per cent. This preparation deteriorates when older than one day. For intravenous use the solution should be filtered and made up to a 3½ per cent. strength, the amount injected may range from 30 to 70 c.c. (1 to 2½ ounces). Not more than 5 grains (0.3 Gm.) of the coagulen are to be employed at any time. (When administered orally, the preparation 5 to 10 grains (0.3 to 0.6 Gm.) is dissolved in milk or tea.) There is no danger of embolism or thrombosis, Fonio claims, but nevertheless he cautions against its use when the patient has impaired vascular walls. Its best indication is in **local hemorrhages**. It is especially valuable when the surgeon can apply or spray coagulen directly to the bleeding area.

**Coagulen** was found by the writer particularly effective for checking all varieties of hemorrhage except that from large arteries. It was applied either as an injection into the region of the bleeding vessels or on tampons or pads of gauze. A 10 per cent. solution in water was prepared fresh and sterilized by boiling. Intravenous injections were of value in uterine bleeding. Vogt (Deut. med. Woch., June 25, 1914).

The writer found coagulen a valuable hemostatic in bleeding carcinomata and post-operative hemorrhages. It is harmless and prompt. It has proven especially valuable in a number of war injuries. In several cases of amputation of fingers, toes, and legs, ligation was dispensed with entirely. Halpern (Beitr. z. klin. Chir., Bd. 95, Hft. 2, 1915).

**DISEASES INFLUENCING THE COAGULATION TIME.**—In certain hemorrhagic diatheses, as hemophilia, the coagulation time may be lengthened to as much as fifty minutes, and in certain purpuras

to ten or fifteen minutes. It would, therefore, be inadvisable to operate under such conditions. In some cases of gall-stones and pancreatic disease in which the coagulation time of the blood is lengthened it is dangerous to operate, because of the difficulties to control the bleeding. In typhoid fever a lengthened clotting time has been found to denote an impending hemorrhage. The coagulation time has also been found to be lengthened in hemoglobinemia, asphyxia, general dropsy, salpingitis, gastric ulcer, jaundice, coal-gas poisoning, and poisoning by bites of certain snakes.

The coagulation time has been found to be shortened after hemorrhage, especially in abortion, carcinoma of the uterus, after transfusion, during starvation, and after the administration of calcium chloride or gelatin.

During the febrile stage of the infectious diseases coagulation is noticeably retarded. The clinical employment of the calcium salts has no direct or invariable effect on the coagulation time of the blood, either in large doses one hour after its administration or in small or large doses at any subsequent period, even extending over two or more weeks. The calcium content of the blood, as determined in terms of ammonium oxalate, proved unreliable. The writers were unable to show definite relationship between leucocytosis and coagulation time. Nucleic acid uniformly failed to produce an increase in the number of leucocytes and also failed to hasten coagulation. But the reaction of the coagulation time to hemorrhage was shown conclusively. They found that citric acid prolongs the coagulation time, and it seemed, even when the difference in time before and after its use was not a very material one, that the viscosity of the blood was lessened. W. E. Robertson, Illman, and Duncan (*Jour. Amer. Med. Assoc.*, May 16, 1908).

The coagulation time of the blood in the circulation seems to be shortened by low barometric pressure, by restriction of fluids, and by exercise;

it is apparently lengthened by increased viscosity and by the taking of food. Among the pathological conditions which are associated with shortening of the time are traumatic hemorrhage, hemorrhage from a uterine carcinoma, severe pulmonary hemorrhage, hematuria, hemoglobinuria, endocarditis, dementia præcox, aneurism, and thrombosis. In the acute stage of typhoid fever, in hemorrhagic disease of the newborn, hemophilia, physiological albuminuria, the acute exanthemata, and possibly in chorea, eclampsia, scorbutus, acromegaly, tetany, acne, eczema, and furunculosis, the coagulation time is lengthened. It appears to be variable in effusions in serous cavities, severe anemia, leucocythemia, jaundice, tuberculosis, convalescence from typhoid fever, pneumonia, rheumatism, nephritis, myxedema, exophthalmic goiter, and epilepsy. Among the exogenous factors shortening the coagulation time are strontium lactate, magnesium carbonate, blood transfusion, pituitary extract (posterior lobe); renal, ovarian, and testicular extracts; possibly persalts of iron, and hydragogues. Lengthening occurs under the influence of citrates, pituitary extract (anterior lobe); extracts of the liver, spleen, pancreas, and suprarenals; chloroform in certain doses, and possibly colchicin, nuclein, betanaphthylamine, atropine, bromides, phosphorus, and curare. No constant effect has been observed after the use of calcium salts, milk, sodium chloride, blood-serum, thyroid extract, thymus extract, alcohol, and gelatin. Myer Solis-Cohen (*Archives of Internal Med.*, Dec., 1911).

The average clotting time of 132 specimens of blood taken from 120 patients suffering from tuberculosis was found to be 7 minutes and 45 seconds. No striking demonstration of results was obtained when these cases were grouped according to coagulation time, occurrence or non-occurrence of hemoptysis, and stage of disease activity or quiescence. A

substudy being made of 24 cases, 12 patients with recent **hemoptysis** showed coagulation time averaging  $8\frac{1}{2}$  minutes. Burns and Young (Amer. Jour. Med. Sci., Dec., 1917).

The writer studied the prothrombin calcium salts and platelets in 45 cases. She found that the coagulation time of **hemophilia** is long. In 1 case reported there was familial hemophilia. The patient's coagulation time was very long; his prothrombin time was within normal limits, and his platelet count was 115,000 per cm. His mother's blood showed an exceedingly long prothrombin time and a normal coagulation time. There was a constant deficiency in prothrombin but apparently no deficiency in calcium in the hemophilia cases. The blood in **epilepsy** seems to show no change in the coagulation time. In **hemorrhagic purpuras** the platelet count was low, and there was no retraction of the clot. Cases of **jaundice** of several weeks' duration showed a marked calcium deficiency and a normal platelet count. In **myelogenous leukemia** the prothrombin time is prolonged and the coagulation time quite short. One patient with **pernicious anemia** showed the prothrombin slightly diminished, and the platelet counts relatively normal. In **splenomegaly** the prothrombin time was delayed, the coagulation time also. Pettibone (Jour. Labor. and Clin. Med., Feb., 1918).

The observation of Stephan and Jurasz that X-ray irradiation of the spleen reduces the coagulation time of the blood was confirmed by the writer. Using the Fanio method at 23 cm. from the skin, 8 minutes, one-third erythema dose, the time reduction averaged 43.4 per cent. Tichy (Zentralbl. f. Chir., 47, No. 46, Nov. 13, 1920).

**COAL-GAS POISONING.** See GASES, POISONING BY.

**COAL-MINERS' DISEASE.** See LUNGS, DISEASES OF: PNEUMONOKONIOSIS.

**COCA, COCAINE, AND COCAINOMANIA.**—*Erythroxylon coca* is a small tree that grows wild in Peru, Bolivia, Brazil, and Ecuador, and is also cultivated in Ceylon and Java. The leaf, which contains the active principles, is the part used in medicine, though these principles are found also in the roots and seeds. The alkaloids present are *cocaine*, *cinnamyl cocaine*, *cocamine* or *truxilline*, and *ecgonine*; there is also a tannin, *cocatannic acid*, which gives rise to a green color in the presence of ferric salts, a wax, and a volatile aromatic principle. In the Javanese variety of coca the alkaloid *tropacocaine* is also found.

Cocaine, or benzoylmethylecgonine [ $C_{17}H_{21}NO_4$ ], the only one of the alkaloids of South American coca that has been found useful in medicine, occurs in colorless, transparent crystals, which are soluble in 5 parts of alcohol and freely soluble in ether and chloroform, but dissolve only in 600 parts of water. The pure alkaloid is insoluble in glycerin, but soluble in 12 parts of olive oil. It has a slightly bitter taste and produces temporary numbness of the tongue.

Upon boiling, cocaine is decomposed into benzoyl ecgonine and methyl alcohol, the former, in turn, in the presence of alkalies, being split into ecgonine and benzoic acid. The view was long prevalent that even a brief period of boiling, such as would take place in the process of sterilizing solutions of cocaine (the hydrochloride), would occasion sufficient decomposition of the alkaloid to reduce perceptibly its analgesic power. Later investigations seem to have conclusively shown, however, that the percentage of drug thus destroyed is

insignificant for practical purposes, unless the boiling be prolonged.

Cocaine forms salts with acids; of the resulting compounds, the hydrochloride is the only one which is official, and this is the substance chiefly used in medicine.

Aqueous solutions of cocaine salts do not keep well unless sterilized and then hermetically sealed. Upon exposure to the air, the solutions develop a heavy growth of molds in a week or two, and are thereby decomposed, with loss of therapeutic efficiency.

### PREPARATIONS AND DOSE.

*Cocaina* (cocaine). Dose,  $\frac{1}{8}$  to  $\frac{3}{4}$  grain (0.0075 to 0.045 Gm.); average,  $\frac{1}{4}$  grain (0.015 Gm.).

*Cocaina hydrochloridum* (cocaine hydrochloride or muriate), occurs either as a white, crystalline powder or as colorless, transparent prisms or flaky leaflets. It is odorless, permanent in the air, and has a slightly bitter, astringent taste. It is soluble in 0.4 parts of water, 3 parts of alcohol and of glycerin, 20 parts of chloroform, and is insoluble in ether. Dose,  $\frac{1}{4}$  grain (0.015 Gm.).

The following preparations of coca were formerly official (U. S. P. VIII):

*Coca* (dried leaves). Required to contain 0.5 per cent. of alkaloids. Dose, 30 grains (2 Gm.).

*Fluidextractum coca* (fluidextract of coca), made by maceration and percolation with dilute alcohol, and subsequent evaporation. Dose, 30 minims (2 c.c.).

*Vinum coca* (wine of coca), containing 65 parts of fluidextract of coca, 75 parts of alcohol, and 65 parts of sugar in 1000 parts of red wine. Dose, 4 fluidrams (16 c.c.).

The following preparation is recognized in the National Formulary:—

*Oleatum cocainæ* (N.F.) (oleate of cocaine), containing cocaine, 5 parts; alcohol, 5 parts; oleic acid, 50 parts, and olive oil, enough to make 1000 parts. Used externally.

Recognized in the former Formulary (N. F. III) were the following:—

*Elixir coca* (N. F. III) (elixir of coca), each fluidram (4 c.c.) representing  $7\frac{1}{2}$  grains (0.5 Gm.) of coca, and consequently  $\frac{1}{24}$  grain (0.0025 Gm.) of cocaine. Dose, 1 fluidram (4 c.c.).

*Elixir coca et guaranæ* (N. F. III) (elixir of coca and guarana), each fluidram (4 c.c.) representing  $7\frac{1}{2}$  grains (0.5 Gm.) each of coca and guarana. Dose, 1 fluidram (4 c.c.).

*Vinum coca aromaticum* (N. F. III) (aromatic wine of coca), each fluidram (4 c.c.) representing about 2 grains (0.125 Gm.) of coca, with aromatics. Dose, 2 fluidrams (8 c.c.).

*Stilus cocainæ dilubilis* (N. F. III) (cocaine pencil), a cylinder of paste about two inches long and one-fifth inch thick, containing 5 per cent. of cocaine. Used for direct application of the drug to skin lesions.

The following unofficial salts of cocaine have been employed for local anesthetic purposes in lieu of the hydrochloride:—

Cocaine sulphate, occurring as a white, crystalline powder, soluble in water and alcohol.

Cocaine phenate (phenol cocaine, cocaine carbolate), occurring in butter-like, partly crystalline masses, insoluble in water, but soluble in alcohol.

Cocaine lactate, occurring as a white liquid of the consistency of honey, soluble in water and in alcohol.

**MODES OF ADMINISTRATION AND EXTERNAL USE.**—

Coca is best administered, if used at all, in the form of a wine or the official fluidextract.

Cocaine hydrochloride may be taken by mouth in dilute solution for its sedative action on the gastric mucosa, or may be administered hypodermically without difficulty for purposes of stimulation in emergencies. Uncombined cocaine (cocaina) is used mainly where a fatty preparation is to be applied externally to relieve pain, as it is soluble in fats, while the hydrochloride is not.

For purposes of local anesthesia, cocaine hydrochloride is used in solutions ranging in strength from 0.01 per cent. (Schleich's method) to 40 per cent. (direct cutaneous anesthesia where the skin is thin). It is also occasionally applied to mucous membranes in crystalline form.

Solutions of cocaine, which offer a favorable nidus for the growth of molds, may be preserved by the addition of salicylic acid or phenol thus:—

**R** Cocaine hydro-

chloride ..... gr. iv (0.25 Gm.).

Distilled water .. ʒiiss (10 Gm.).

Salicylic acid ... gr. ½ (0.01 Gm.).—M.

For the sterilization of cocaine solutions intended for hypodermic injection or instillation, various methods have been suggested. The most convenient plan is to put up the solution in aseptic ampoules made of glass as free from alkali as possible, seal the ampoules, and then heat them in the autoclave for half an hour at 110° to 115° C. (230° to 239° F.). They will then keep indefinitely, with the initial loss of but a small fraction of their analgesic power. For solutions to be painted or sprayed on mucous

membranes, vials—likewise preferably free from alkali—may be filled with the cocaine solutions, stoppered with sterile cotton, and boiled in water the boiling point of which has been slightly raised by the addition of common salt or glycerin. The vials should, of course, not be left open after use. In summer, if they are drawn from daily, the solutions should be changed once every fortnight (Le Mée).

In minor operations the best results were obtained with a 1 per cent. solution of cocaine pasteurized at 60° C. (140° F.) for three hours. Cocaine solutions of the same strength pasteurized at 80° C. (176° F.) and at 120° C. (248° F.) for two hours and for fifteen minutes, respectively, gave far less satisfactory anesthetics. Pasteurized solutions gave anesthesia lasting an hour or two, while sterilized solutions (boiled at 100° C.—212° F.) gave a freedom from pain for from twenty to thirty minutes. Krymoff (Roussky Vrach, Aug. 16, 1903).

The writer never failed to secure anesthesia with a small amount of the solution after boiling it. Also there have been no undesirable effects, such as irritation of the cornea or conjunctiva, and the healing of surgical wounds has not been interfered with in any way. Virden (Amer. Jour. of Surg., Aug., 1915).

Cocaine solutions can be sterilized in a current of steam without decomposition for three-quarters to one hour, provided the sterilization is carried out in alkali-free glass containers. Ebert (Amer. Med., Dec., 1917).

**INCOMPATIBILITIES.**—The hydrochloride of cocaine in solution is incompatible with hydroxides, carbonates, and bicarbonates of the alkali metals, which precipitate the relatively insoluble uncombined cocaine—except in solutions more di-



lute than 1:600—by combining with the acid radicle. The heavier metals forming insoluble chlorides, such as mercury and silver, would cause precipitation not only of cocaine hydrochloride, but of the alkaloid itself. The iodides, iodine, and sodium borate are also incompatible with cocaine.

**CONTRAINDICATIONS.**—The contraindications to cocaine correspond practically to those of local anesthesia in general. Coca itself can hardly be said to have any definite contraindications, and cocaine is used chiefly for the purpose mentioned.

Local anesthesia is absolutely contraindicated only where the technical difficulties involved in securing it are insuperable. The relative contraindications vary greatly according to a number of circumstances, such as the experience of the surgeon with the procedure, the time at his disposal in the individual case, known idiosyncrasy to cocaine on the part of the patient, etc., and can only be stated in a general way. Braun has epitomized the most important of the relative contraindications in the statement that "children and adults who behave like children are not good subjects for local anesthesia."

According to Matas, anesthesia with cocaine or its allies is oftenest impracticable: (1) in operations in which complete muscular relaxation is required, as in the reductions of fractures and dislocations of the larger bones and joints; (2) in extensive atypical operations on the head and trunk in which the regional method is inapplicable and the operative field cannot be well defined or circumscribed, as in the radical extir-

pation of mammary cancer by Halsted's and Meyer's methods; (3) in atypical operations involving prolonged and complicated maneuvers in the splanchnic cavities, especially when the organs operated upon are adherent and inflamed; (4) in all operations upon patients whose emotions are beyond the control of reason or the will, as in the violently insane, in delirious patients, in children, in hysterical and extremely timorous patients.

As suggested by Mortimer, delicate operative procedures, *e.g.*, those carried out on the eye, should not be undertaken under local anesthesia in patients who are deaf.

In cases where the physical examination which should always precede anesthesia discloses circulatory weakness, there is particular interest in the substitution for cocaine of one of the newer, less toxic, analgesic drugs, such as novocaine or quinine and urea hydrochloride.

**PHYSIOLOGICAL ACTION.**—**Locally**, cocaine has little or no action upon the unbroken skin, but it produces complete local anesthesia when applied to the mucous membranes or subcutaneous tissues. The part at first becomes blanched after the application of the drug, but this is not the cause of the anesthesia. As Richet has remarked, current observation affords frequent illustration of the fact that analgesia may be present without complete anemia of the part. Analytic experiments show that cocaine locally applied, while a strong vasoconstrictor, possesses a special affinity for the peripheral nerve-tissues, in which it tends to produce temporarily a complete loss of function. Curiously, not all forms

of nerve-terminations are alike paralyzed, however; sensations of heat or cold, and mere tactile impressions, are recognized where all sensitiveness to pain has been abolished. It is an accepted fact that the effects of the alkaloid are not limited to the nerve-endings, but involve all the finer nerve-fibers with which it comes in contact.

Cocaine applied distally to nerve-fibers picks out and paralyzes some fibers before others, the sensory before the motor, the vagus fibers conducting upward before those conducting downward, the vasoconstrictors before the vasodilators, and the bronchoconstrictors before the bronchodilators. Dixon (*Jour. of Physiol.*, Dec. 30, 1904).

Experiments on frogs and rabbits which showed that cocaine and, still more, stovaine affect the neurilemma and change it in a specific manner. The myelin and also the neurokeratin are more or less altered, and in some of the nerve-fibers were found altogether destroyed. The findings indicate a special affinity between the poisons and certain elements of the neurilemma, which favors the penetration of the drug through the protecting sheath to the conducting elements of the nerve. Santesson (*Nordiskt med. Arkiv*, xxxix; *Intern. Med.*, No. 3, 1907).

Cocaine first increases the activity of unstriated muscle and then depresses it, whatever be the nature of sympathetic control. The writer ascribes the dilatation of the pupil caused by cocaine to a direct action on the muscle of the iris. Kuroda (*Jour. of Pharm. and Exper. Therap.*, Nov., 1915).

Taken into the mouth, cocaine, besides causing a subjective feeling of numbness and astringency, abolishes the sense of taste, though here, too, there is evidence of the dissociation of different peripheral nervous func-

tions in that salty substances are more easily recognized by the incompletely cocainized tongue than bitter ones, such as quinine. Applied intranasally, cocaine temporarily removes the sense of smell. On all mucous membranes, its power to prevent or relieve pain stands in close relation to the tenuity of the membrane itself, thin membranes being penetrated and anesthetized with great rapidity. The more quickly it enters, however, and the greater the vascularity of the subjacent tissue, the more rapidly it is absorbed into the general circulation, its local anesthetic action thereupon promptly disappearing. The advantage of combining a small amount of epinephrin with cocaine employed locally, in order to prolong the effect of the latter, is thus rendered evident.

The primary vasoconstriction produced by cocaine is followed, on disappearance of the effects of the drug, by a secondary dilatation of the vessels, frequently to a point beyond the normal, whence the appearance of the area treated may change from one of pallor to abnormal redness.

Although its effect on peripheral nervous structures is the predominant feature of its local action, cocaine is classed as a "general protoplasmic poison," in the sense that the life of all forms of tissue may be destroyed by it when it is applied to them in suitable concentration. This property is illustrated by the paralyzing effect of the drug on the leucocytes and on ciliated epithelium, as well as by the tendency of unduly strong solutions of it to injure the superficial cellular layer of the cornea and to favor infection and necrosis of the tissues when injected subcutaneously, as in cocainomaniacs. Sometimes a

preliminary stage of increased functional activity precedes that of paralysis. Cocaine is powerfully toxic to infusoria, but hardly at all to bacteria.

**General Effects.**—*Nervous System.*

—When taken internally, or otherwise absorbed into the organism, coca and its alkaloid produce a sense of exhilaration and increased readiness for exertion similar to that caused by large doses of caffeine. There is a marked tendency to restlessness and wakefulness, a feeling of augmented mental and physical power, and an absence of hunger. These phenomena, except the last-named, are due to stimulation of the central nervous system, including both the brain and the spinal cord. With moderately large doses the reflexes are exaggerated; a further increase may induce tremors, and, when the dose is toxic, convulsions, chiefly of the clonic or epileptiform type, are likely to supervene, followed, in turn, by central nervous depression.

The peripheral nerves and their endings can be influenced but little or not at all in man by cocaine taken internally. Death from respiratory paralysis would occur before enough of the drug could be absorbed to develop this effect. In the frog, however, in which arrest of the respiratory movements is not fatal because the respiratory function is subserved to an important extent through the skin, the peripheral nervous effects of cocaine, both on the sensory and motor structures, can be demonstrated. Ritter has found it possible to produce complete general analgesia in dogs by intravenous injections of large doses of cocaine. Harrison has definitely proven, however, by experimentation on himself, that this

procedure is unapplicable in man. Upon application of a solution of cocaine to a nerve-trunk, or its injection in the vicinity, temporary paralysis of the fibers of the nerve is produced owing to penetration of the alkaloid into their midst. If the amount present be not too great, subsequent recovery of the nerve without injury of any kind will take place. In the mean time, however, a condition of complete "nerve-block" will have existed, in which neither motor nor sensory impulses—supposing the nerve to be a mixed one—could travel through the segment paralyzed. It is characteristic of the drug that the sensory paralysis should occur sooner and with weaker solutions than the motor, a fact which is ascribed to a greater selective affinity for the former class of fibers. That such a difference should exist need not surprise us, since, as has already been stated, the effect even on different forms of sensation varies in intensity.

*Circulation.*—In moderate doses cocaine slightly stimulates the heart, acting either directly on the heart muscle or through the accelerator mechanism. More marked, however, is the exciting action of the drug on the vasoconstrictor center in the medulla, which brings about a marked degree of general vascular narrowing, perhaps further assisted by a direct effect of the cocaine on the vessel walls themselves. As results of these actions there occur a more or less marked quickening of the heart rate and a rise in the blood-pressure. Toxic doses of cocaine, on the other hand, after temporary stimulation of the circulatory functions, tend to slow and weaken the heart action, a fall of blood-pressure.

also taking place. The heart is particularly sensitive to intravenous injections of cocaine, showing marked depression even with comparatively moderate amounts.

Effects of cocaine on heart of mammals studied. Minute amounts of cocaine added to perfusion fluid passed through the coronary vessels in Langendorff's method cause the heart to beat more strongly but more slowly than normal. This is the first phase in the action of the drug. With larger amounts—2:100,000—there occurs, after the preliminary action already mentioned, diminished systole and pulse rate. A further increase in the quantity of drug causes from the outset slowing of the beats and weakening of the pulse. This is the third phase, or that of beginning paralysis. The irritability of both the myocardium and epicardium is greatly diminished. Amounts of cocaine ranging from 30 to 50:100-000 cause ultimate arrest of the heart in diastole. At any stage of the action, the substitution of cocaine-free fluid for that previously perfused causes a more or less complete return of the cardiac functions to normal, according to the degree of intoxication reached. M. Kochmann and F. Daels (*Archives inter. de pharm. et de thér.*, xviii, Nos. 1 and 2, 1908).

*Blood.*—Maurel has shown that the leucocytes undergo changes under the influence of cocaine, at least *in vitro*, and has even suggested that these changes may be concerned in the local anesthetic effect of the drug. A 0.02 per cent. solution, he found, causes these cells to swell up to over twice the normal size and to assume a spherical shape. Although the leucocytes no longer adhere to the vessel walls, their great size, coinciding with the diminished lumen of the capillaries due to direct vasoconstriction, will result, he contends, in com-

plete obliteration of these vessels,\* with consequent interruption of nutrition and abolished sensibility of the structures previously supplied with blood through them. More serious effects, such as pulmonary embolism, may also be produced through the distribution of the enlarged leucocytes in the blood-stream. The red corpuscles are not affected by the drug.

*Respiration.*—Full doses of cocaine strongly stimulate the respiratory centers in the medulla. The rate of breathing is greatly increased, in animal experiments often to over twice the normal figure. The depth is at first about as before, but later diminishes, the breathing sometimes becoming very shallow. After poisonous doses, the rate is secondarily slowed, especially during convulsive seizures, and death may promptly take place from asphyxia.

Cocaine is the most prompt and efficient of all respiratory stimulants. The writer gives  $\frac{1}{2}$  grain (0.03 Gm.) hypodermically, repeating the dose as required. Two illustrative cases are cited: one of alcoholism with threatened respiratory failure and semi-comatose for 2 days; the other was a case of acute paraldehyde poisoning whose breathing had been reduced to 6 to 8 per minute. Pettey (*So. Med. Jour.*, Apr., 1914).

*Eye.*—When applied to the eye or taken internally in large doses cocaine acts as a mydriatic and impairs accommodation. The pupillary dilatation is not attended with loss of the light reflex, thus indicating that the oculomotor nervous control of the iris is not paralyzed, as is the case with atropine, and, since, in addition, cocaine will cause further dilatation of the pupil after atropine has been applied, it is generally conceded that

the effect of the former is a stimulation of the dilator nervous mechanism of the iris, i.e., the sympathetic or autonomous terminals.

Anesthesia and some pallor of the cornea and conjunctiva are also caused by direct application of cocaine. Where the solution applied exceeds 4 per cent. in strength, roughening and even slight cloudiness of the cornea may result. This is not due merely to temporary arrest of winking, which allows the cornea to become dry, since the other local anesthetics do not cause it; it is produced mainly through destruction of the superficial cells of the cornea by the cocaine. The vessels of the iris are sometimes markedly narrowed by this agent.

Another effect which is very characteristic when large amounts are injected or locally applied is exophthalmos. This is attributed to the stimulating action of the drug on the sympathetic system.

*Muscles.*—When a relatively moderate dose of cocaine is injected into a frog in which the blood-supply to one of the hind limbs has been previously cut off by a ligature, and the work which the two gastrocnemii are able to perform is compared by exact methods after a suitable time has been allowed for absorption of the drug, it is found that the contractions of the cocainized gastrocnemius upon electric stimulation are slightly more marked than those of the cocainized muscle, and generally, too, the endurance of the former preparation is the greater. This difference may also be observed when the drug is directly applied to one of the muscles after both have been removed from a pithed frog. There is

therefore apparently a special stimulating effect of cocaine on voluntary-muscle tissue.

It is not generally believed, however, that the increased muscular power and resistance to fatigue shown by the Indians of Bolivia and Peru who chew coca leaves when on the march are due to the direct effect of the alkaloid on the muscles, but to that on the central nervous system. It has, indeed, been shown that the cortical motor areas are excited by weaker electric stimuli after the administration of cocaine than before.

*Alimentary Tract.*—Cocaine tends to remove the appetite, probably by paralysis of the nerve-terminals in the stomach.

According to von Anrep, cocaine, unless given in very large amounts, increases intestinal peristalsis.

Baldacci and Guido have found absorption to be noticeably diminished in parts of the intestine treated directly with cocaine.

*Temperature.*—Cocaine tends to raise the body temperature, especially if given in supratherapeutic doses, when the rise may amount to several degrees C. According to Reichert, this is due to an increased production of heat, which is caused in two ways: (1) through the motor excitement resulting from excitation of the cerebral cortex, and (2) through direct stimulation of the thermogenic center in the caudate nuclei. In animals in which the spinal cord at its junction with the medulla and the crura cerebri has been cut, no rise of temperature is produced by cocaine. Reichert considers cocaine and morphine directly antagonistic in their action upon the centers related to heat production.

**Secretions.**—Cocaine may either decrease or increase the secretions; its tendency appears to be rather toward the former effect.

**Metabolism.**—Large amounts of the drug have been found to cause rapid emaciation in rabbits. The urea elimination is simultaneously diminished, and that of imperfectly metabolized nitrogenous substances is increased. In mice, Ehrlich has observed cocaine to cause fatty changes in the liver-cells and even necrosis.

Cocaine introduced subcutaneously into dogs causes a temporary but significant increase in body temperature. With daily doses of 10 mg. ( $\frac{1}{4}$  grain) of cocaine hydrochloride to each kilo ( $2\frac{1}{4}$  pounds) of body weight for short periods of time, no influence can be detected upon nitrogenous metabolism nor upon fat utilization, but when daily injections of 15 mg. ( $\frac{1}{4}$  grain) are administered fat utilization is slightly impaired and body weight is considerably decreased. Underhill and Black (Jour. of Biol. Chemistry, April, 1912).

**Absorption and Elimination.**—Cocaine is rapidly absorbed from mucous membranes, but is almost incapable of penetrating the horny layer of the skin.

In the lower animals cocaine is almost completely destroyed in the system. The degree to which this takes place in the human organism, however, is as yet unknown. According to Pouchet, cocaine is rapidly eliminated with the urine and bile.

**UNTOWARD EFFECTS AND POISONING.**—Man is peculiarly sensitive to the general action of cocaine. Furthermore, there is so much variation in the susceptibility of different individuals to this alkaloid, and in the phenomena of intoxication witnessed, that it is justifi-

able to divide cases of poisoning into two classes: those induced by small amounts in persons with an idiosyncrasy, and those arising from the absorption of toxic doses of the drug.

In the former variety of cases, the characteristic phenomena are those of syncope. The patient becomes dizzy, later partially or completely unconscious, and there is pallor, slow and shallow respiration, and feebleness or absence of the pulse, though the rate of the heart beats is increased. The forehead may be moist with perspiration. These effects are chiefly of spinal and sympathetic origin, and result from the marked peripheral vasoconstriction and cerebral anemia thereby engendered. They occur most frequently in adolescents or young adults of both sexes,—16 to 25 years, according to Garel,—as well as in the aged. Jackson Clarke has reported the case of a man aged 65 in whom as little as  $\frac{1}{40}$  grain (0.006 Gm.) of cocaine, injected hypodermically, brought about faintness and nausea.

Case of a boy of 14 years with high myopia. It was decided to "needle" the lenses. The operation was, as usual, carried out under local anesthesia, a few drops of 5 per cent. cocaine being instilled into the eye. Each time after the needling the boy vomited. Vomiting does occasionally supervene after needling when the tension of the eye becomes markedly increased, but in this case there was no increase of tension. The supposition of cocaine idiosyncrasy seemed more reasonable. J. Allan (Prescriber, Sept., 1912).

Case of intolerance for a very small dose of cocaine, characterized by fever and organic nervous and cardiac symptoms, followed later by trophic disturbances of the fingers and disturbances of the equilibrium

when standing. Tobias and Kroner (Berl. klin. Woch., Feb. 18, 1918).

In cases of acute cocaine poisoning caused by relatively large amounts of the drug, mental excitement, an exaggerated sense of well-being, loquacity, incoherence, and actual delirium are typical features. A period of motor restlessness, with slight inco-ordination and accelerated pulse and respiration, is sometimes observed. The patient complains of headache, vertigo, and occasionally dryness of the throat. The pupils at the same time dilate, the reflexes are exaggerated, and tremors may occur. Vomiting is an occasional symptom. After very large doses, epileptiform convulsions are likely to appear very soon. Simultaneously or shortly after, circulatory and respiratory depression assert themselves, the pulse becoming feeble, the respiration more and more slow and irregular, and the skin cold and cyanotic. If the dose be a lethal one, death takes place generally through failure of the respiratory centers, abetted by cardiac and vasomotor weakness, or, possibly, through tetanus of the muscles of respiration during a convulsive seizure.

Case of a young woman aged 22 years, eight months advanced in pregnancy, in whom marked symptoms due to cocaine addiction were masked by and mistaken for those due to pregnancy. She had been taking the drug for nearly two years, the habit originating from a friend's advice to rub a little cocaine on the gum for toothache. She appears to have taken at one period 30 to 60 grains (2 to 4 Gm.) or more *per diem*. The chief symptoms that occurred during the six months previous to her death were enlarged pupils, nausea, and at times great depression of spirits. Though without a real crav-

ing for alcohol, she was constantly thirsty, especially in the morning, when she often had to take much water or lemonade. About six months before death she had an attack described as "a very bad faint," probably due to excess of cocaine, as the symptoms were somewhat similar to those of the ultimate fatal attack, i.e., faintness, cyanosis, and twitching of face and extremities. H. E. Knight (Quarterly Med. Jour., May, 1900).

A patient under treatment for the morphine habit who was known to be very susceptible to cocaine received by the mouth 30 mg. (about  $\frac{1}{2}$  grain) of that substance. The pulse, normally weak and never faster than 80, rose to 104 and became hard and tense. A noticeable feature was the enlargement of the outline of the heart, with marked palpitation, which occasioned much alarm to the patient. The case terminated in recovery. J. Hofmann (Therap. Monats., No. 11, 1901).

A patient had swallowed by mistake  $11\frac{1}{2}$  grains (0.75 Gm.) of cocaine, and was soon in a condition of extreme tachycardia and dyspnea. Gradual recovery took place in about two weeks. It was found that large quantities of phenolglycuronic acid were excreted, because, as a result of the cocaine poisoning, the powers of oxidation were diminished and the body was unable to oxidize the sugar as it would have done normally, as well as the glycuronic acid due to the presence of the cocaine and the camphor which had been administered as a stimulant. J. Wohlgemuth (Berl. klin. Woch., Oct. 10, 1904).

A girl of 12 met death in forty seconds from a hypodermic injection of 12 drops (0.7 c.c.) of a 4 per cent. solution. Zemp (Cited by J. M. French, Amer. Jour. of Clin. Med., June, 1908).

Case of poisoning occurring after 2 applications of a 2 per cent. solution of cocaine to the throat and tonsils within an hour. A. G. Gibson (Lancet, Feb. 26, 1910).

Case of serious poisoning following an injection into the gums of a mixture of cocaine, phenol, and tincture of iodine, prior to the extraction of five teeth. Notwithstanding symptoms of collapse, the operator repeated the injection the next day, when eleven more teeth were extracted. The patient was seriously ill for nearly five months, being unable to walk and suffering from profound general debility. A fatal termination was narrowly escaped. The writers believe the heart muscle was severely damaged by the poison. Price and Leakey (*Lancet*, March 25, 1911).

The writer urges anew the fact that adrenalin and cocaine must be used with very great care and discrimination. Many authors are quoted who have observed sudden death follow the injection of cocaine-adrenalin solutions during a chloroform anesthesia. Aikins (*Canad. Pract. and Rev.*, xli, 96, 1916).

The duration of a case of severe acute cocaine poisoning is in many instances shorter than with most other alkaloids. The patient either promptly succumbs or is soon out of danger. Even after comparatively mild cases, however, unpleasant effects, such as mental imbalance, insomnia, anorexia, irritability, and cardialgia (Pouchet), are likely to be present for some days after the intoxication.

Case of a woman about 48 years of age who had some teeth extracted by a dentist who used about 15 drops (0.9 c.c.) of an 8 per cent. solution of cocaine. Probably this quantity was used for each of the four or five teeth extracted. Strychnine and atropine were given hypodermically. About one hour after the symptoms of cocaine poisoning had appeared the following condition was observed: Dilated pupils; tongue partly protruded; eyes closed, and all symptoms of the head resembling very much a deep

narcosis by chloroform. There was no reflex of the eyes and all the functions of the brain were suspended. Pulse full and strong, and only a little more rapid than normal. Respirations about 26, full, and easy. The patient's position was changed by rolling and lifting her from side to side of the bed without any sign of disturbance. Free vomiting had previously occurred. As the pulse remained full and strong and the atropine caused a flush of the face, the remedies were not repeated, and only a mustard plaster to the occiput added. About the time, however, it was intended to repeat the strychnine, there was a sudden change, announced by a weak, rapid pulse and stertorous breathing, and death followed in a few minutes.

The dentist had on a previous occasion extracted several teeth, operating while she was under the influence of the same formula and dose that he had used on the last occasion, without any bad results. C. D. R. Kirk (*Med. Brief*, Dec., 1908).

Case of a soldier who had a urethral fistula secondary to a stricture. An attempt was made to pass a bougie after injecting into the urethra a little of a 10 per cent. solution of cocaine, the urethra being compressed between the finger and thumb behind the stricture. The solution was allowed to escape when the syringe was removed. After five minutes, more cocaine was injected in the same manner. Three minutes later, while the stricture was being dilated, the patient's color became very bad, and a convulsion lasting half a minute occurred. The necropsy showed a few cauliflower vegetations on the mitral valve, which, however, acted perfectly.

In another case death followed the introduction of a small amount of a 10 per cent. solution into the urethra to facilitate the use of the urethroscope. Jameson (*Jour. of the Royal Army Medical Corps*, May, 1910).

Case of fatal cocaine poisoning in a man of 52 after local anesthesia for



a herniotomy. It was found that a 10 per cent. solution of cocaine had been injected by mistake instead of the supposed 2 per cent. novocaine solution. The bottles were kept on the same shelf, with the same size, shape and color of label. The sudden death was unexplained at first, all measures having failed. Moller (Ugeskrift f. Laeger, Oct. 31, 1918).

The average convulsive dose of cocaine in persons not unusually susceptible may be stated as 3 grains (0.2 Gm.), and the lethal dose does not greatly exceed this. It is to be borne in mind, moreover, that as little as  $1\frac{1}{2}$  grains (0.1 Gm.) have been known to produce death in an adult. In the use of cocaine for purposes of local anesthesia it is inadvisable to inject or apply more than  $\frac{1}{2}$  or at most  $\frac{3}{4}$  grain (0.03 or 0.045 Gm.) of the drug.

The writer observed repeatedly from minimal doses of cocaine (Schleich's infiltration narcosis), mild symptoms of poisoning. Dentists have had a large number of deaths from this. He gives every patient, without exception, 25 to 50 c.c. ( $6\frac{1}{4}$  to  $12\frac{1}{2}$  drams) of **whisky** or **cognac**, by the mouth, before the first injection of cocaine. In long-continued operations he repeats the dose, mixing the whisky with sugar water in women and children. In 4 years he has had no trouble. Herzfeld (Zentralbl. f. Chir., xl, 1705, 1913).

**Treatment of Acute Cocaine Poisoning.**—In the syncopal form of cocaine poisoning, *i.e.*, that resulting from the employment—generally for local anesthesia—of relatively small doses in susceptible individuals, the first procedure indicated is to place the patient in **recumbency**, with the head thrown slightly backward and the feet elevated. Rapidly acting, stimulating measures, such as **inhalations of ammonia**, ingestion of **hot**

**coffee**, with a few teaspoonfuls of **brandy**, and injections of **ether**, **camphorated oil** or **strychnine**, should next be applied. **Slapping the face and chest with cloths dipped in hot or cold water** may also be availed of. Several authors have recommended the inhalation of **amyl nitrite**, 2 to 6 drops (0.12 to 0.3 c.c.), in order to relieve the vasoconstriction caused by cocaine; the evanescent effect of this measure may be prolonged by giving a hypodermic injection of 2 or 3 minims (0.12 or 0.18 c.c.) of **spiritus glycerylis nitratis**.

When a local application causes pallor, vertigo, or faintness, 1 dram (4 c.c.) of **aromatic spirit of ammonia** in 2 ounces (60 c.c.) of water affords relief.

In the more severe cases of cocaine poisoning, due to massive doses, the **stomach** should be **evacuated**, either by washing it out or with an emetic, if the poison has been taken by the mouth. **Tannic acid**, 20 to 30 grains (1.3 to 2 Gm.) in water, or **strong tea**, may be given as a precipitant. To prevent convulsions, if the case be seen early, full doses of **chloral hydrate** and **bromides** may be given by mouth. The former drug will also tend to remove the vasoconstriction produced by cocaine. Psychic excitement, if marked, may be combated with **morphine**,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.015 to 0.03 Gm.) hypodermically, and will also be influenced by the **chloral**, a decided antagonist. Convulsions should be treated by careful **chloroform** or **ether anesthesia** and the administration of **chloral hydrate**, 45 to 60 grains (3 to 4 Gm.), and **potassium bromide**, 1 to 2 drams (4 to 8 Gm.), by rectum.

Animals poisoned by cocaine can be saved by means of **inhalations of chloroform**; but they show marked

changes in their internal organs afterward. The animals were ill for a week or two, and great care was required to secure their permanent recovery. Parine (Roussky Vratsh, May 27, 1906).

The action of strychnine and morphine in counteracting cocaine is too slow in dangerous cases. The most effective treatment is to administer **ether by inhalation**. Cases which seemed hopeless were thus saved, the depressing effects of cocaine on the heart and respiratory system being antagonized almost instantly. The ether should be administered only to the degree of mild surgical narcosis, or even less. A mask should always be employed and the anesthetic given by the drop method. J. E. Engstadt (Jour. Amer. Med. Assoc., March 19, 1910).

Strychnine, an adrenal stimulant, should never be used, according to Sajous, whose emergency treatment is the use of **amyl nitrite**, followed by hypodermic injections of **nitroglycerin**. Both agents counteract the peripheral constriction of the arterioles which cocaine produces by stimulating the adrenals.

Circulatory or respiratory depression should be carefully watched for, and, as soon as it appears, combated by stimulants, such as **caffeine sodio-benzoate**, 5 grains (0.3 Gm.) hypodermically, or **hot coffee**, 8 ounces (250 Gm.) by rectum; **digitalis**, **camphorated oil**, **alcohol**, etc.

Bozza found by experimentation in animals that, if the minimum fatal dose of cocaine hypodermically be taken as 1, there can be injected without fatal result (a)  $\frac{1}{2}$  of the dose, if the injection be followed by **saline hypodermoclysis**, or (b)  $\frac{1}{3}$  of the dose, by **intravenous saline infusion**. An even more marked difference was observed where the drug had been

administered by the mouth. It would seem, therefore, that this measure might prove useful in cocaine poisoning in the human subject.

In cases where the drug has been injected under or into the skin, an effort should be made to prevent further absorption, either by **constricting the root of the limb** or by applying cold to the **area of injection**.

Le Mée, having in view Maurel's theory of the leucocytic swelling and embolism in cocaine poisoning, advises that the **breathing be artificially aided**, in order to assist the lungs in getting free of the dead corpuscles; that the resisting power of the remainder be increased by the ingestion of **hot fluids** and by **hot baths**, and that **air heated to 104° F. (40° C.)**, which is a strong vasodilator agent, be breathed by the patient.

In desperate cases, **oxygen inhalations** should, if possible, be given. Ingraham considered oxygen "the only true antidote to cocaine."

In cases of acute cocaine poisoning in which the drug has been taken internally, the **stomach** should be **washed out** at once. Respiratory failure is to be met with **alcohol**, **camphor**, **aromatic spirit of ammonia**, and perhaps **oxygen** and **artificial respiration**. A rapid injection of **normal saline** has proved beneficial. Yawger (N. Y. Med. Jour., Dec. 3, 1910).

**Chronic Cocaine Poisoning.**—For a discussion of the "cocaine habit" the reader is referred to the special section on Cocainomania at the end of this article.

**THERAPEUTICS.**—The therapeutics of this drug may be conveniently discussed under two headings, referring respectively to the internal and the local modes of administration. The internal or systemic uses

will first be summarily referred to, and the consideration of the more important external modes of employment afterward taken up.

**A. Internal or Systemic Uses.**—As a **gastric sedative**, cocaine is not infrequently of value in vomiting due to irritation or other disturbance of the mucous membrane of this organ. It has been chiefly employed in the **vomiting of pregnancy**, in **postoperative vomiting**, and in **seasickness**. In the first-named disorder from  $\frac{1}{2}$  to 1 wineglassful of coca wine or, in the more obstinate cases,  $\frac{1}{2}$  to 1 dram (2 to 4 c.c.) of the fluidextract of coca may be taken three or four times daily. In postoperative vomiting Crandon advises that 5 to 15 minims (0.3 to 1 c.c.) of a 2 per cent. solution of cocaine hydrochloride be given in a teaspoonful of hot water every half-hour for 3 or 4 doses; this, he has observed, will sometimes allay a most persistent case. In seasickness, Rockwell used successfully in several cases 5 minims (0.3 c.c.) of a 4 per cent. solution of cocaine repeated every hour or two until 3 doses had been taken; the cocaine was preceded by catharsis.

In disorders of the stomach associated with pain, especially gastric carcinoma, cocaine has been used for its analgesic property. Such employment of the drug is, however, to be strongly deprecated, as there is available a number of better agents, in particular orthoform and anesthesin, which, while almost equally effective, and with a more prolonged action, eliminate the danger of increased tolerance and craving for the drug, an advantage of no mean importance.

**As Stimulant to Medullary Centers.**  
—In the presence of shock and in

**poisoning by narcotics**, cocaine may prove of considerable value as a respiratory and vasomotor stimulant. Moderate doses only should, however, be used, as large doses are apt to be followed by pronounced secondary depression, which is superimposed upon that originally present. The dose should be  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.008 to 0.016 Gm.) hypodermically, and the latter amount should not be repeated more than once or at most twice, lest more harm be done than good. Cocaine should seldom be depended upon alone, and is mainly useful as an adjuvant to other stimulating remedies. Combined administration of cocaine and strychnine affords a particularly powerful exciting effect on the respiratory centers.

**As Nerve Stimulant and General Tonic.**—In persons suffering from **fatigue**, coca is found to renew the mental and physical powers, giving a feeling of comfort and well-being, and making possible the endurance of further work and stress. Similarly, in those who are about to undertake unusual exertions, the preparations of this drug act as powerful stimulants. Coca wines have been especially employed for these purposes, and it has been claimed as an advantage for them that, while containing small amounts of cocaine, their effect was partly due not to this alkaloid, but to related substances, such as cocamine and benzoyl ecgonine, which exert a relatively greater stimulating effect directly on the muscles than cocaine and less on the central nervous system. Overindulgence in the use of coca is, nevertheless, strongly advised against, in view of the danger of habit formation unless a prepara-

tion can be obtained which does not contain cocaine. Since the Council on Pharmacy and Chemistry of the American Medical Association has taken up the question, a Mariani wine has been prepared which is guaranteed free of cocaine, a fact which renders it the safest preparation available.

In various nervous disorders, especially **neurasthenia** and **melancholia**, the fluidextract and wine of coca have sometimes given satisfaction, the stimulating action of the drug quickly bringing about subjective betterment. Especially have the small doses thus absorbed proven advantageous where there was a loss of appetite and impaired digestion. The habit is, however, an ever-present possibility, in neurotics especially, and the utmost care should be exercised in employing the remedy.

The use of cocaine in morphine habit is referred to only to be condemned, experience having shown that a double habit is frequently the ultimate result.

**B. Local Uses.**—The pronounced local analgesic properties of cocaine render it an invaluable agent for the performance of minor operations as well as, under certain circumstances, of more extensive ones. The drug is also employed for the relief of established pain, to relieve congestion and irritability of mucous membranes, *e.g.*, in the nasal cavities, to control hemorrhage, and as a mydriatic. These less important uses will be considered first, and local anesthesia reserved for the end of the article.

**To Relieve Established Pain.**—The pain in **sciatica**, **intercostal neuralgia**, and all forms of **muscular rheumatism** may be temporarily overcome by the

hypodermic injection of cocaine. In all cases except those of neuralgia of the head and face,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 Gm.) may be injected over the seat of pain; where the head is the seat of pain, the injection may be made into the arm, though much of the drug's efficiency is thereby sacrificed. In nearly all cases treated the pain disappears almost completely for some hours, after which, if it returns, it is generally in a milder form. The chief disadvantage of this procedure is the associated danger of habit formation, especially if the injections are frequently repeated. This danger is avoided if some of the less toxic substitutes for cocaine, especially novocaine, be used.

In the palliative treatment of **hemorrhoids** and **anal fissure**, cocaine is of value as an analgesic and vasoconstrictor. Similarly, in the **tenesmus** of dysentery cocaine may be used to relieve the excessive irritability of the rectum. Jelks employs the following suppository in **amebic dysentery**:—

**R** *Cocaina hydrochloridi*,

*Ext. stramonii*,

*Ext. belladonnæ fol.* ãã gr. ss (0.03 Gm.).

*Olei theobromatis* .... q. s.

M. et ft. in suppos. no. j.

Sig.: Hold the suppository in the anal canal about a minute; then press into rectum with finger.

In **ocular inflammations** associated with pain, or in the presence of a **foreign body** which is greatly irritating the conjunctiva, the instillation of 2 or 3 drops (0.12 or 0.18 c.c.) of a 1 or 2 per cent. cocaine solution is considered permissible by some, provided the cornea be not diseased, and gives marked relief. Others, however, dissent from this view.

Cocaine should not be given for overcoming pain in the eye, because its effect is only temporary. The patients drop it in the eye too often, and corneal injuries result. For operation or with conjunctival injections the author uses cocaine in association with epinephrin and morphine hypodermically. Schleich's infiltration anesthesia is not recommended for operations on the eyelid. Cocaine is useful for photophobia and mydriasis. In place of cocaine for controlling the pain, warm or cold compresses, leeches, or dionin are ordered. Fuchs (Wiener klin. Woch., Sept. 18, 1902).

In severe **earache** a drop (0.06 c.c.) of the fluid produced by mixing phenol, menthol, and cocaine crystals in equal parts may be instilled in the meatus (Ballance).

In **herpes zoster** cocaine was used locally in 23 cases by Bleuler, who asserts that it not only relieved the pain, but also caused a regression of the eruption, which disappeared in a few days. The affected surface was painted with equal parts of wool-fat and petrolatum, rubbed up with 1 per cent. of cocaine hydrochloride, and dressed with linen spread with the same ointment.

**To Relieve Congestion and Irritability of Mucous Membranes.**—When applied to a mucous membrane, cocaine, in addition to producing anesthesia, causes a temporary blanching and shrinkage by constricting the blood-vessels.

In **acute coryza** cocaine in 2 per cent. solution, carried over the nasal mucous membranes by means of an applicator, or used with caution as a spray, will cause the turgid tissues rapidly to subside and relieve for a time the unpleasant stuffiness. It may also check the excessive secre-

tions. The insufflation every two hours of a small amount of a powder consisting of cocaine hydrochloride, 1 part; bismuth subcarbonate, 5 parts, and talc, 15 parts, is also effective under these conditions. It is unfortunately a fact, however, that the effect of cocaine is followed by a more or less marked secondary dilatation of the vessels. Further, if the applications be frequently repeated, tolerance rapidly sets in, the benefit procured becomes less, and the habit may be established. The only absolutely safe plan therefore is *never to place cocaine in the patient's hands*, and, if its employment be considered advantageous, for the physician to apply it himself, either with a pledget of cotton, when a solution is employed, or by means of an insufflator, if a powder is required.

In **chronic rhinitis** and **ozena** the application to the membranes of cocaine phenate in 1 per cent. or stronger solutions in 30 per cent. alcohol has been recommended.

In **hay fever** spraying of the nasal mucosæ (by the physician only) with a 4 per cent. cocaine solution, preferably rendered feebly alkaline, will temporarily relieve the excessive local irritability. It should be immediately followed by a spray of liquid petrolatum, which acts as a protective with the addition of **menthol**, 10 grains (0.6 Gm.) to the ounce, to perpetuate the anesthetic effect.

**Photophobia** is temporarily relieved by cocaine. In the presence of corneal ulceration, however, its continuous use is unwise, as the vitality of the corneal tissue will be lowered by it.

The Eustachian catheter is more easily introduced after the application

of a solution of cocaine to the nasal cavities and nasopharynx. For diagnostic purposes also, cocaine is useful, in that by contracting the blood-vessels it renders more prominent distinctions between hypertrophy of the intranasal soft tissues and tumors of cartilaginous or bony character. Nasal and laryngeal polypi are more easily diagnosed with the aid of cocaine. Epinephrin is, however, even more powerful than cocaine in its shrinking effect on mucous membranes.

In minor hemorrhages, *e.g.*, in epistaxis, cocaine in 4 to 10 per cent. solution may be used as a local hemostatic; but there is some liability to a later return of hemorrhage, owing to the vasodilation which follows the subsidence of its effect.

In operations performed under local anesthesia the vasoconstrictor effect of cocaine is of considerable assistance to the operator. Through the temporary control of the hemorrhage it affords, the field of operation is rendered clearer and more open. This effect of cocaine is greatly augmented by the simultaneous use of a small proportion of epinephrin, which not only controls hemorrhage, but by causing extreme constriction of the vessels slows the absorption of the cocaine, thereby prolonging its local effect and diminishing the chances of unpleasant general symptoms.

**As Mydriatic.**—Cocaine, used in 2 to 4 per cent. solution, is a good mydriatic. Its cycloplegic action is, however, very feeble; hence it is not available for refraction work and is of value only where pupillary dilatation is alone desired.

**LOCAL ANESTHESIA.**—This is by far the most important use of

cocaine. The term "local analgesic," strictly speaking, more correctly, describes the effect sought and obtained, as it is especially upon the pain sense, as distinguished from the temperature and general tactile senses, that this drug acts.

The chief disadvantage of cocaine is its *high toxicity*, which renders it necessary that great care be exercised not to apply or inject more than a certain amount, if untoward symptoms are to be avoided. The limit compatible with safety is commonly placed at  $\frac{1}{2}$  to  $\frac{2}{3}$  grain (0.03 to 0.04 Gm.) for adults.

Invaluable as *local anesthetics* are, they *carry in their path many a danger*. A small portion of the fluid always gets into a vein or lymph duct and may be carried quickly into the circulation. In non-fatal cases one may merely notice a slight faintness, a small pulse, and heavy breathing. In more severe cases there are cold perspiration, dryness in the throat, a feeling of impending dissolution, hallucinations, laughter, unconsciousness, epileptiform attacks, coma, and finally paralysis of the respiratory center. Weigand found that in 17 intoxications occurring after application of cocaine to the nasal mucosa there was no fatal result; in 12 poisonings after the application in the mouth and pharynx, 2 deaths resulted, and in 11 poisonings after anesthetizing the larynx, 1 death. G. B. Wood observed that in about 10 per cent. of his patients in whom **adrenalin** had been applied in full strength, secondary vasomotor relaxation occurred. B. Seymour Jones had 3 cases showing the alarming effect of the sudden absorption of adrenalin on the septum when the circulatory system was depressed by chloroform.

The writer warns against injecting any cocaine or adrenalin preparations into the turbinated bodies, for the absorption is too rapid and the

dangers are too many. For removal of the tonsils most operators, however, use cocaine-adrenalin injections into the crypts and around the organ. But several deaths have been recorded in the literature, and perhaps many more have occurred unrecorded. The writer uses for injections a solution consisting of  $\frac{1}{2}$  to 1 per cent. cocaine, plus adrenalin (1:10,000). In the present state of the question he does not feel safe in using a stronger solution.

One may almost make it a rule that the slower adrenalin is injected, and the more diluted it is, the less danger there will be. W. Freudenthal (Med. Rec., July 20, 1912).

**Indications.**—For local anesthesia these vary in some degree according to the skill and confidence of the surgeon or anesthetist in this form of procedure, but may be said to comprise, in general, brief operations in superficial areas of small size, *e.g.*, the amputation of fingers, the removal of benign new growths, etc. In patients whose general condition is so poor, however, as to involve unusual risk in ordinary inhalation anesthesia, the indications for local anesthesia may extend to major operations, many of which, including laparotomy, have been thus performed with complete success. Other indications are afforded by the absence, in an emergency, of a suitable anesthetist, or the danger attending general anesthesia in the presence of certain special conditions, such as pronounced anemia, diabetes mellitus, or empyema. The patient's temperament, too, must be remembered as an important factor in deciding as to the propriety of local anesthesia. Where there is any doubt as to the success of the method in a given case, preparations should be made as though a general anesthetic were to be given,

and ether or chloroform administered if the occasion so demands (Mortimer).

The writer uses tablets containing cocaine hydrochloride, 0.05 Gm. ( $\frac{3}{4}$  grain), and epinephrin, 0.00016 Gm. ( $\frac{1}{400}$  grain), are sterilized by dry heat for an hour on three successive days and can then be preserved indefinitely. By dissolving a tablet in sterile salt solution a perfectly fresh and isotonic solution is obtained. Only two strengths are needed, viz., a 1 per cent. solution for nerve blocking and a 0.1 per cent. for ordinary infiltration. In general, local anesthesia is available whenever the whole field of operation can be rendered anesthetic. Forty per cent. of all operations were performed with cocaine alone, and an additional 12 per cent. were assisted by a little chloroform or ether, making a total of about half of all the cases. These included amputation of limbs, wiring of fractures, excision of glands of neck and groin, excision of rib, trephining, osteotomy, thyroidectomy, excision of breast, excision of varicose veins of leg, perineal urethrotomy, suprapubic cystotomy, circumcision, excision of hemorrhoids and fistulae, exploratory laparotomy, cholecystotomy, appendectomy, colostomy, typhoid perforation, radical cure of hernia, varicocele and hydrocele, and many minor procedures. Mitchell (Jour. Am. Med. Assoc., July 20, 1907).

Even in the absence of special contraindications to cocaine (see Contraindications) it has been advised that the patient about to be subjected to cocaine anesthesia should be given daily 20 to 30 grains (1.3 to 2 Gm.) of a bromide on the three days preceding the operation, and that just before the intervention he should drink a cup of hot coffee in order to produce a hyperemia of the medulla and brain which will counteract the tendency of cocaine to produce ischemia of these structures (Le

Mée). All tight clothing should be removed, and, wherever practicable, the patient operated while recumbent. Morphine may be given.

**Hyoscine hydrobromide**,  $\frac{1}{400}$  grain (0.00065 Gm.), given by mouth over 800 times before operations under cocaine; 1:1000 to 1:5000 cocaine is used for infiltration, and never is a solution over 2 per cent. in strength applied for operations upon mucous membranes, such as submucous septal resections. The patients prepared with hyoscine are minus the usual fear, always in good condition, and, owing to the lasting effects of the drug, are free from pain for several hours. Hyoscine, like atropine, possesses antidotal properties when administered before cocaine. It counteracts cocaine in those cases when cocaine poisoning arises unexpectedly while the cocaine is being given in what are considered physiological doses. Hyoscine hydrobromide delays the effects of cocaine on the heart, until the cocaine is introduced in such quantities as to poison the heart muscle itself. Myron Metzenbaum (Ohio State Med. Jour., Dec., 1910).

The writer injects a small dose of **morphine** before starting the anesthetization, when about to operate on acutely inflamed tissues, or when for any other reason he anticipates that such pain will follow. In aseptic cases it is rarely necessary to repeat the injection toward evening. In ambulant practice he prescribes a mixture of **morphine and aspirin**, or **pyramidon** in 2 powders, one to be taken as soon as the pain appears, the other if needed later for sleep. Aspirin or pyramidon alone is given when pain is not to be expected. F. Honigsmann (Zentralbl. f. Chir., Jan. 31, 1914).

**Novocaine and adrenalin** for local anesthesia is readily performed. For minor operations, or when working in a home, sterile tablets of from  $\frac{1}{8}$  to 1 grain (0.02 to 0.06 Gm.) are employed, and are ready as soon as dis-

solved in sterile water. In hospital practice, for an ordinary **hernia** or **laparotomy**, 2 to 3 ounces (60 to 90 Gm.) of a 0.5 per cent. solution, to which is added 6 to 10 drops of a 1:1000 adrenalin solution, is prepared by first boiling the crystals of novocaine and later adding adrenalin. A fresh solution is made for each operation. The maximum dose of novocaine is variously given as from  $7\frac{1}{2}$  to 22 grains (0.48 to 1.4 Gm.). Bechtol (Jour. Ind. State Med. Assoc., Dec. 15, 1915).

The following methods of procuring analgesia with cocaine are employed:—

(a) **External Application**.—This method is utilized especially for anesthesia of mucous membranes, although a few authors have pointed out the possibility of securing an adequate anesthesia of the skin in areas where the latter is very thin by applying a strong solution of cocaine.

Beach found that if a 40 per cent. freshly prepared solution of cocaine is applied from one to one and a half hours to the unbroken skin, local anesthesia results. **Circumcision** may, for instance, be accomplished without pain in this way.

**Nasal Cavities**.—A 5 to 10 per cent. solution of cocaine hydrochloride is generally painted repeatedly over the mucous membranes. The weaker solution should be used first (Gongna), then the stronger, and both should be carried evenly over the surface by gentle rubbing. According to some, a 4 per cent. solution is sufficient for all ordinary purposes, and it is even stated to produce a more marked and lasting insensibility than the stronger solutions. For short operations involving only a limited area, a 1:2000 epinephrin solution may with advantage be first applied for ten minutes,



and a saturated solution of the cocaine then rubbed in, particular attention being paid to the line along which the membrane is to be incised.

Anesthetic mixture employed for **submucous resection** consisting of about 20 to 25 grains (1.3 to 1.6 Gm.) of cocaine crystals, to which sufficient epinephrin hydrochloride solution, 1:1000, is added to dissolve the crystals. The solution is applied as follows: The cotton on the applicator is wet so that there is no excess of solution, and the entire field of operation swabbed over. One can then operate for three-fourths hour without the slightest discomfort to the patient. F. E. Miller (Med. Rec., Feb. 23, 1907).

Another method of applying cocaine is to dip one end of a thin layer of absorbent cotton in the solution. Introduce this extremity first into the nasal cavity, and, while holding it against the mucous membrane deep in the forceps, draw the excess of solution over to the dry portion by compression with another smooth forceps, and press the whole of the cotton against the area to be anesthetized. In this manner the least possible amount of cocaine is used, and, although, in general, a 2 to 5 per cent. solution is sufficient, a 10 or even 20 per cent. solution may be employed where turbinates or septal spurs are to be removed. Epinephrin, 1:3000, may be added to the foregoing solution.

Cocaine sprays for the nose need not exceed 1 per cent. in strength. Special care should be taken as to the amount of solution used,—often a matter of some uncertainty.

Harland found that cocaine in spray form can safely be employed if limited to a few gentle puffs of a 1 per cent. aqueous solution. If used

on the cotton-tipped applicator, a 5 per cent. solution should be the maximum strength employed.

In none of the above procedures should more than  $\frac{3}{4}$  grain (0.05 Gm.) of cocaine be applied, as absorption is relatively complete. Wherever possible, indeed,  $\frac{1}{2}$  grain (0.03 Gm.) should not be exceeded. Any of the drug felt by the patient to enter the pharynx should be expectorated by him. It is stated that the analgesic power of cocaine solutions in general is increased by heating them before use to from 104° to 113° F. (40° to 45° C.). Guisez and Garel also advocate the addition of alcohol in the proportion of 2.5 to 25 per cent. to cocaine solutions, having found the analgesic activity to be augmented thereby.

In a person weakened by age or illness, and whose circulation is poor, absorption of cocaine from the nasal mucosæ may take place so slowly as to tempt the operator to deluge the tissues in order to hasten the local relief. In such a case, after absorption is completed, poisoning may be expected to occur.

The writer protests against the increasing tendency to perform operations upon the nose and throat under general anesthesia. In adults it is seldom necessary to resect the nasal septum, or remove the tonsils, to say nothing of operations upon the turbinates or the ethmoid, except with local anesthesia.

Perfect *ischemia and anesthesia* may be obtained by carefully packing the nose with equal parts of a 10 per cent. solution of cocaine, and a 1 to 1000 solution of **adrenalin**, 1 hour before operation, and the sense of shock may be abolished, as Crile has shown, by the use of **morphia** combined with **atropine**, and, in selected cases, with **hyoscine**. If the operator

prefers the injection method, he should use **novocaine**,  $\frac{1}{4}$  per cent., with the addition of not more than 6 minims (0.36 c.c.) of 1:1000 solution of **adrenalin** to each dram (4 Gm.). The injection should be made about 15 to 30 minutes before operation. Whenever possible, a solution of novocaine should be selected instead of cocaine, as it has toxicity of one-tenth that of cocaine. Wishart (Can. Pract. and Review, Jan., 1916).

**Pharynx and Larynx.**—Here sprays or insufflations are generally preferred to direct applications with cotton, especially in the case of the larynx, where all unnecessary local irritation is to be avoided. A 10 per cent. solution of cocaine hydrochloride may be sprayed into the larynx twice at an interval of two or three minutes, after which an applicator should be brought in contact with the organ from time to time until it is found that all local irritability has been abolished. The operative procedure intended should then be promptly carried out, as the anesthesia is only of short duration. The amount of cocaine permissible in anesthesia of the larynx is larger than in the case of the nasal cavities, as toxic symptoms are less readily induced from the former area. The limit for laryngeal use is placed by Lermoyez at  $1\frac{1}{2}$  grains (0.1 Gm.), though it is, of course, safest to remain as far below this as possible.

Where it is intended to cauterize **infected ulcers**, the mucous membrane may be first rendered partially insensitive by insufflation and then, if desired, Bonain's fluid, consisting of a mixture of cocaine, menthol, and phenol in equal parts, applied (Le Mée).

For anesthesia of the tonsillar regions, submucous injections of 1 or

0.5 per cent. cocaine are generally preferred to external applications; they will be discussed later. (See Hypodermic Method.)

In the pharynx proper a 3 per cent. solution may be sprayed on the mucous membrane two or three times.

**Ear.**—A large number of methods for securing analgesia of the external meatus and drum membrane have been advocated. One of the most useful plans where only a relative degree of insensibility is required is to insert a 10 per cent. ointment of cocaine (alkaloidal) in hydrated wool-fat; for rapid analgesia this should be rubbed into the skin of the meatus, whereas for prolonged effects, as in **earache**, it should merely be placed in the canal, absorption thus occurring slowly.

For deep anesthesia of the drum membrane or tympanum a 20 per cent. solution of cocaine hydrochloride in water may be left in contact with the parts for ten minutes, or crystals of cocaine applied; or, again, one of the special analgesic mixtures may be employed.

Gray's mixture, consisting of 1 part of cocaine hydrochloride in 10 parts each of aniline oil and 95 per cent. alcohol, is effective only if the external auditory canal is absolutely dry; 10 drops will generally induce profound anesthesia in fifteen minutes. More reliable is Bonain's fluid, as modified by its originator:—

**R.** *Pure phenol*  
(crystalline),  
*Menthol* (crystalline),  
*Cocaine hydrochloride*,  
of each ..... gr. xv (1 Gm.).  
*Epinephrin chloride* ..... gr.  $\frac{1}{64}$  (0.001 Gm.).—**M**

This is applied on a small wad of cotton to the tympanic membrane, with which it is left in contact for three to six minutes. Alcohol should not be used either before or after paracentesis when this mixture is applied, as its caustic power is thereby increased. Where there is perforation, considerable care is necessary in using this mixture.

Analgesia sufficient for the removal of **aural polypi** may be secured by placing cotton wet with a 4 per cent. cocaine solution in contact with the parts for five minutes (Gleason). In more painful operations, however, such as **ossicectomy** and procedures requiring incision in the meatus, a mixture in equal parts of 1 per cent. cocaine and 1:1000 epinephrin should be injected with a hypodermic syringe beneath the skin of the meatus at the junction of the bony and cartilaginous portions.

*Eye.*—In the eye cocaine hydrochloride is used in solutions of from 0.5 to 4 per cent. strength, with or without epinephrin 1:2000, 1 to 5 drops (0.06 to 0.3 c.c.) being instilled once or repeatedly, according to the depth of analgesia required. It is employed before operative procedures, as well as in the presence of a **foreign body** or to relieve pain due to **acute inflammation**. In the presence of keratitis its use is not advisable, however, since it has been known to produce permanent opacities of the cornea. Even where the cornea is normal, the stronger solutions of cocaine tend to cause drying and roughening of its epithelium. To avoid this effect in so far as is possible the eyelids should be kept closed after the drug has been dropped in. Boric acid, 1 or 2 per cent., is fre-

quently added with advantage to cocaine solutions intended for ophthalmic use. For deep local anesthesia crystals of cocaine may be used.

To secure complete anesthesia for operating upon the iris of the eye put a few drops of cocaine into the conjunctival sac; then at the point where the fixation forceps will be placed, and opposite where the incision is to be made, inject a few drops of 5 per cent. cocaine beneath the conjunctiva, but not into the episcleral tissues. After five or six minutes operation can be performed. Koller (Brit. Med. Jour., Nov. 12, 1904).

Beta-eucaine hydrochloride, 2 per cent.; alypin, 2 per cent., and holocaine, 1 per cent., are not infrequently used in preference to cocaine in anesthesia of the eye, owing to the absence of effect on the corneal epithelium, iris, and ciliary muscle. For prolonged relief from pain, as well as for other purposes, dionin in 1 to 5 per cent. solution has also been employed.

The effect of cocaine in the eye comes on generally in five to eight minutes, and persists about ten minutes, after which the instillations may be cautiously repeated. The cornea, conjunctiva, and iris are all anesthetized. The pupil is dilated, but still reacts to light. The power of accommodation is but slightly affected. Some degree of exophthalmos and broadening of the palpebral fissure may be noted.

*Genitourinary Tract.*—The injection of a few drops of a 2 per cent. solution of cocaine into the urethra renders **catheterization** painless, provided no stricture be present. **Operations on the bladder**, as well as **ureteral catheterization**, are rendered painless through previous injection of

cocaine, but *solutions stronger than 2 per cent. should not be used*, as fatal poisoning has followed the injection of 5 drams (20 Gm.) of a 5 per cent. solution into the urethra.

In anesthetizing the urethra the author cleanses the glans, places a  $\frac{1}{2}$ -grain (0.032 Gm.) tablet of cocaine in the meatus, and then makes the tablet damp by means of a drop of sterilized water, thus forming a paste. A bougie is then carried through the paste along the whole urethra into the bladder. Wether- spoon (Interstate Med. Jour., July, 1903).

The writer observed a case in a man of 46 who had had his appendix removed. That night, 2 unsuccessful attempts at catheterization were made, slight bleeding following. Two hours after the last trial, 3 drams (12 c.c.) of a 4 per cent. cocaine solution were injected into the urethra. The patient at once had a convulsion and died. As is usual, nothing characteristic was shown at autopsy. Death occurs so promptly that it is almost impossible to counteract the action of the anesthetic. Ellis Kellert (Jour. Labor. and Clin. Med., Dec., 1918).

For application to the mucous surfaces of the vulva, vagina, and the uterine cavity, 10 to 20 per cent. solutions of cocaine are employed. Their use should be confined to minor operations,—**curettage, dilatation of the cervix, removal of uterine polypi**, etc. In operations extending beneath the surface parenchymatous injections of the analgesic should supplement the external applications.

Cocaine used as a preliminary to cauterization of **chancroids**. The drug is useful in other ways than as an anesthetic. A tablet containing  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.032 Gm.) of the drug converts the ulcer within a few minutes into a vascular, healthy surface from which exudes a bloody

serum. It is rubbed into the ulcer lightly with a swab. The application is of great service in sluggish sores. The *rationale* of the method is the same as that of the Bier method: Infection cannot long withstand the hyperemic assaults. The formula found especially serviceable for use by the patient was: *Cocaine hydrochloride*, gr. xx (1.3 Gm.); *animal charcoal*, 3j (4 Gm.). This is to be applied twice a day, after cleansing the ulcer carefully with hydrogen peroxide and drying thoroughly. G. Frank Lydston (Jour. Amer. Med. Assoc., Feb. 24, 1912).

*Other Regions.*—Cocaine solutions may be applied previous to cauterization of the buccal mucous membrane, as in certain forms of **stomatitis**.

In the performance of **esophagoscopy** a 10 per cent. solution should first be applied to the glossoepiglottic fossæ, pharynx, and glottis itself; two or three minutes later, a 20 per cent. solution is applied at the upper outlet of the esophagus, and afterward in the course of the canal, as required. Similar applications are to be made before **tracheobronchoscopy**, but when once the trachea is entered no solution stronger than 5 per cent. should be used, as rapid absorption takes place from its mucous membrane (Le-Mée).

For the cauterization of sensitive **skin ulcerations** in general, cocaine solutions may also be employed as analgesics.

(b) **Injection with Hypodermic Needle.**—This method is employed where incisions are to be made through relatively thick and impermeable surface layers, especially the skin, and where anesthesia is to be obtained deeply beneath certain mucous membranes, viz., those of the tonsillar region and rectum. These

mucous membranes will first be referred to, and cutaneous anesthesia then discussed.

**Tonsils.**—Sterile cocaine solutions of 0.5 to 4 per cent. strength are used for local anesthesia of the faucial tonsils, the solutions being injected with a hypodermic syringe into both anterior and posterior pillars in three places, as well as into the supratonsillar fossa and the tonsil itself. Care should be taken never to exceed  $\frac{1}{3}$  grain (0.021 Gm.) of cocaine for each tonsil, as phenomena of intoxication are easily induced; in fact, it is best to keep well below this limit. Gleason uses tablets containing  $\frac{1}{6}$  grain (0.01 Gm.) of cocaine and  $\frac{1}{300}$  grain (0.0002 Gm.) of epinephrin. If the tonsils are large 2 tablets are dissolved in 20 minims (1.25 c.c.) of water, whereas if they are small or the patient is weak, but 1 tablet is used.

Analgesia of the pharyngeal tonsil is best secured by first applying a 20 per cent. cocaine solution for the purpose of contracting the inferior turbinate, and eight minutes later injecting into the tonsil a 0.5 per cent. cocaine solution in 8 per cent. sodium chloride.

**Rectum.**—In rectal operations especial caution is necessary in the amount of cocaine used, as untoward happenings have occurred even from the injection of a few drops of 4 per cent. cocaine. Fortunately, it is a fact that solutions of only 0.1 to 0.5 per cent. strength are capable of producing a sufficient analgesia in this region, provided enough pressure be simultaneously exerted on the sensory nerve-endings by distention of the tissues with the fluid; hence the stronger solutions formerly used have been largely discarded.

The rectal operations most frequently performed under local anesthesia are those for **hemorrhoids**, **fissure**, small **perianal abscesses**, simple and shallow **fistulæ**, and the excision of **condylomata**, **sebaceous cysts**, and **dermoids** of the anal region. Hirschman prefers a 0.1 to 0.5 per cent. solution of beta-eucaine lactate to cocaine in these cases. Where the sphincter is to be dilated previous to the operative procedure the needle is entered at a point posterior to the anus and the fluid injected on either side of the orifice at a distance of about one-half inch from it, a U-shaped wheal of infiltration being thus formed, which soon permits of painless mechanical dilatation of the anus. The analgesic solution is then injected into or beneath the tumor or ulceration to be dealt with, and the operative intervention then carried out.

The writer advocates local anesthesia by novocaine and adrenalin, using the technique evolved and very successfully employed by Prof. Recus, as follows:—

*Novocaine* .....  $7\frac{1}{2}$  gr. (0.5 Gm.).  
*Adrenalin* 1:1000 gtt. xxiv.  
*Physiolog. saline*  
*sol. steril.* ....  $3\frac{1}{8}$  oz. (100 c.c.).

Fifty to 80 c.c. ( $1\frac{3}{4}$  to  $2\frac{3}{4}$  ounces) of this solution can be injected without any ill effects.

The patient is purged the day before operation, shaved and prepared for operation in the usual way. After being placed on the table in the exaggerated lithotomy position, a pledget of cotton saturated with the novocaine-adrenalin solution is carried into the rectum with the aid of a pair of artery forceps. This procedure is repeated until several pledgets have been inserted, and these are left *in situ* until injection of the external structures is complete. A glass syringe with a half-curved

rather stout and long hypodermic needle is used for injecting the field of operation. The muco-cutaneous margin encircling the anus should first be injected, after which the needle should be inserted at the base of the swelling caused by the fluid inserted in the injection. This procedure is repeated until a ring of injected fluid surrounds the anus. The pledgets of cotton are now removed from the rectum, and the operator proceeds to inject the internal sphincter muscle. To accomplish this purpose the forefinger of the left hand is hooked behind the sphincter muscle, which is pulled forward and steadied; a long straight-needle attached to the syringe is pushed perpendicularly to the skin into the muscle, and a series of injections are made encircling the bowel as in the superficial external tissues already described. H. Treves-Barber (Louisville Monthly Journal, Oct., 1914).

The hydrochloride of quinine and urea is another analgesic drug which, like eucaïne, has become a formidable rival to cocaine in rectal surgery. Distention of the tissues with distilled water can be used as a substitute for cocaine in internal hemorrhoids.

Performance of many operations on the **cervix**, both in gynecology and obstetrics, with local anesthesia by means of cocaine advocated. Four injections of cocaine into the cervical tissues are given in front, behind, and on the sides with an amount of solution which will equal 4 cg. ( $\frac{1}{2}$  grain) of cocaine. In four or five minutes there is perfect local anesthesia. This method is applicable in all operations on the cervix: repair, incision of cysts, dilatation for treatment, curettage, and prolapse operations. After labor the removal of adherent membranes and dilatation for rapid evacuation of the uterus may be done. F. Fèbres (Presse méd.; Med. Rec., April 27, 1912).

*Skin in General.*—A needle of as fine a caliber as possible should be employed in giving anesthetizing injections of cocaine, as in quickly thrusting such a needle through the skin practically no pain is produced. Where a very fine and sharp needle cannot be obtained, or absolute painlessness is desired, the part to be operated on after the preliminary antiseptic cleansing may be sprayed with ethyl chloride until insensibility is produced, or a drop of pure phenol may be applied at each point through which the needle is to be inserted. A drop or two of cocaine solution is then injected in various places, each producing an area of analgesia within the edges of which other injections may subsequently be made, thus gradually increasing the extent of the insensitive area.

A solution of 1 or 2 per cent. strength, injected either hypodermically or into the Malpighian layer of the skin (Reclus's method), will produce anesthesia of the surface sufficient to permit of painless incision. Where the injection is subcutaneous, analgesia does not occur at once, whereas if it be made obliquely into the dermis itself immediate insensibility is caused through paralysis of the nerve-endings both by the drug and the pressure exerted by the solution, which produces a circumscribed, white elevation of the superficial skin layers.

Nerves, no matter how small, should never be handled before cocaineization; to do so will lessen the confidence of the patient in the method, cause unnecessary pain and a certain amount of shock. For a similar reason lacerated and contused wounds of the extremities should not be prepared for operation

previous to cocainization. The addition of epinephrin is unnecessary when weak cocaine solutions are used; it increases the tendency to secondary oozing of blood into the tissues. The point of the needle should always be in sight (intraepidermal); otherwise, an unnecessary amount of solution will be required to anesthetize the sensory-nerve terminals. It is impossible to insert the needle too superficially. Watson (Jour. Oklahoma State Med. Assoc., Aug., 1910).

In the excision of small **superficial tumors** or **cysts**, the anesthetizing fluid may be first injected intradermally in an area covering and surrounding the line of the intended incision, then subcutaneous injections made beneath the growth. A similar procedure may be carried out for the opening of small **superficial abscesses** and **boils**, with the proviso that the injections are not to be made into the inflamed tissues themselves, as the separation of the latter induces intense pain.

Where an incision is not the sole operative measure to be accomplished the mere injection of cocaine is inefficient, as the drug is rapidly carried away by the blood, especially after subcutaneous injections, the analgesia promptly disappearing. Various methods have therefore been sought and proposed for prolonging the action of the analgesic. These are based chiefly upon *anemia of the part to be anesthetized*.

Corning was the first to show that by arresting the arterial and venous circulation in a limb the effect of an injection of cocaine can be prolonged to ninety minutes, if necessary. The limb is first exsanguinated with an *Esmarch bandage* carried up to, but not beyond, the field of operation.

Another bandage or tourniquet is then placed circularly around the limb above the seat of operation, the first bandage removed, and the injection of the anesthetic begun. Pels-Leusden has, however, tried the practice of putting the band in place only *after* the field of operation has been injected, and believes that anesthesia is accelerated thereby. By these methods the danger of poisoning from the cocaine is practically eliminated, as the drug does not enter the general circulation during the operation and what remains can later be allowed to enter it gradually by slowly or intermittently loosening the bandage.

Thus, in operations on the fingers and toes, as for **whitlow** or **ingrowing toe-nail**, after the member has been encircled at its base, injections of 1 per cent. cocaine hydrochloride may be made both anteriorly, posteriorly, and laterally, with special attention to the vicinity of the nerve trunks. Anesthesia is obtained after about ten minutes. The distribution of the fluid through the tissues may be hastened by gentle massage of the part. The quantity of cocaine injected should, if possible, not exceed  $\frac{1}{4}$  grain (0.015 Gm.).

Another means of facilitating anesthesia through anemia of the tissues is the addition of a small proportion of *adrenalin* to the solution to be injected. The action of the analgesic drug is so favored thereby that the concentration required to produce a given degree of effect is diminished. Especially in the case of analgesics other than cocaine, such as stovaine and novocaine, is this co-operation of value, as these agents do not, like the former, themselves induce vasocon-

striction. The freedom of the field of operation from exuded blood is, of course, an additional advantage. As generally employed, the epinephrin produces in five to ten minutes after injection an ischemia extending one-half to one inch beyond the area treated (Parker).

Mixture of 5 per cent. cocaine hydrochloride solution with 1:1000 solution of epinephrin in the proportion of 2 drops to each c.c. (16 minims) of the cocaine solution employed in 45 cases, including **lipoma** of the external genital organs, **phlegmon**, **epithelioma** of the left cheek, **cancer** of the lower lip, **atheromatous tumors** of the forehead, **fistula** of the lower jaw, etc. In all there was complete anesthesia, with an entire absence of any parenchymatous hemorrhage, the anesthetic effect being observed on the diseased tissues also. Piletzky (Rous-sky Vrach, Feb. 25, 1905).

Mixture of 9 parts of 0.5 per cent. cocaine hydrochloride solution and 1 part of 1:1000 epinephrin hydrochloride recommended for small surgical operations. Repeated injections are made about the region to be incised, up to 10 c.c. (160 minims) of the fluid being used. Anesthesia is produced in seven or eight minutes. Gangitano (Archives Ital. de Biol., March, 1905).

Conclusion reached after many experiments on guinea-pigs that epinephrin would not protect the organism from toxic doses of cocaine. Berry (Amer. Jour. Med. Sci., Oct., 1905).

Contrary to some recent teachings, epinephrin injected with or even before cocaine does not lessen its toxic action. The effect of cocaine was not at all increased by the addition of epinephrin, and just as much cocaine was required if epinephrin was added as without it. The anemia produced by epinephrin is, however, a great advantage, and it should always be used when hemorrhage is

feared. The accentuation of spinal anesthesia by the addition of epinephrin is due to the anemia of the cord, which in itself produces anesthesia of the limbs. Sikemeier (Archiv f. klin. Chir., Bd. lxxvii, Heft 2, 1906).

Mixture of cocaine and epinephrin employed in 328 operations. A uniform mixture of 6 Gm. (96 minims) of a 1:1000 solution of epinephrin; 0.3 Gm. (5 grains) of cocaine hydrochloride, and 60 Gm. (2 ounces) of distilled water was used. This mixture can be boiled two or three times without impairing its anesthetic properties. The writer warns against secondary capillary hemorrhages, which may occur after the effects of the epinephrin have worn off. In **circumcision** the solution should be introduced into the margin of the prepuce, between the two layers thereof, 1 Gm. (16 minims) of the mixture being enough. For **ingrown-nail** operations it is unsuited, as the procedure of injection is too painful. It is preferable for this operation to ligate the base of the toe tightly with an elastic band and freeze the entire operative field with ethyl chloride, whereupon the nail can be removed painlessly by introducing a spatula under it. Zartsine (Roussky Vrach, Oct. 14, 1906).

In cocaine-epinephrin local anesthesia, to induce a maximum degree of anesthesia and ischemia with a minimum of general drug absorption, it is necessary to use solutions of high density, which do not readily enter the larger blood and lymphatic glands. The diluting effect of the mucous-membrane secretions must be borne in mind, and cotton-wound applicators should be frequently changed and freshly charged with the anesthetizing solution. Before beginning to operate one should carefully test every part of the field with a probe to determine whether the anesthesia is complete. It is difficult to anesthetize when bleeding has once begun, and the patient will



greatly appreciate the extra effort made to spare him needless pain. Leshure (N. Y. Med. Jour., Feb. 6, 1909).

Cocaine is superior to eucaine and other similar preparations. The author uses a 0.5 per cent. solution of cocaine hydrochloride in sterile water, to 100 c.c. (3½ ounces) of which are added 3 minims (0.18 c.c.) of fresh epinephrin hydrochloride (1:1000). The mixture is stocked in sterile colored bottles, each holding 10 c.c. (160 minims), with a glass stopper sealed with wax. Sealed bottles remain unimpaired for at least two months, but a solution which has been exposed to the air should never be used again. A 0.25 per cent. solution of cocaine is in reality sufficient for nearly all purposes. The author has frequently used 2 ounces (60 c.c.) of a 0.5 per cent. solution. Braithwaite (Practitioner, Feb., 1911).

*Injection into the vicinity of nerve trunks* (conduction or regional anesthesia) is a valuable means of increasing the efficiency of hypodermic anesthesia. According to the procedures of Oberst and Hackenbruch, 0.5 to 2 per cent. solutions of cocaine or novocaine, with or without 1:20,000 epinephrin, are introduced in such situations as to block the afferent nerves from the field of operation. This method gives a prolonged anesthesia and permits of accurate work in the field of operation, since there is no edema of the tissues dissected. In operating on a finger, Oberst, after applying a constricting bandage, produces a circular zone of infiltration just below it, inserting the needle only twice,—at the dorsal and palmar surfaces of the finger. The nerve trunks coursing in the subcutaneous tissues are thus blocked and thorough anesthesia is produced. If a 1 per cent. solution of cocaine be used,

not more than ⅛ to ⅓ grain (0.01 to 0.02 Gm.) of the drug need be injected in operating on fingers or toes by this method (Gehardi). Hackenbruch, operating, e.g., upon a circumscribed lesion on the forearm, injects the solution in an hexagonal figure (necessitating only three needle punctures) almost or completely around the area to be operated, thus similarly cutting off the nerve-supply, without producing an edema of the field of operation or raising the skin in lumps.

The Oberst method is practically limited to the digits and adjoining parts, regions not well adapted to Schleich's infiltration method. The method is easy, satisfactory, and entirely free from danger. In anesthetizing a finger, a tourniquet is first applied at its base. Soft-rubber tubing answers well; nor is great pressure needed, since the circulation of the finger is readily arrested. After it is applied, 5 to 10 minims (0.3 c.c.) of a 1 per cent. solution of cocaine are injected around each digital nerve distal to the tourniquet. After ten minutes the entire finger distal to the tourniquet is completely anesthetic, and operation on it from a small incision to an amputation may be done painlessly. When the base of the finger requires operation the constricting band may be applied at the wrist. The cocaine should then be injected on the palm and dorsum of the hand along the lines of the digital nerves. Struthers (Edinburgh Med. Jour., Aug., 1903).

Oberst's method of cocaine injection for **operations on the penis** described. A small rubber tube or catheter is placed around the organ at the penoscrotal junction and drawn moderately tight. The penis is washed with bichloride and placed on a clean towel, or preferably a square of white glazed paper. The needle, having been placed in boiling water for two minutes, is attached to a

clean syringe, into which is drawn a fresh solution of cocaine hydrochloride, 1 per cent. The needle is thrust into the tissue of the corpus cavernosum, and about 5 minims (0.3 c.c.) of the solution are deposited. It is then withdrawn, and about 5 minims (0.3 c.c.) more are placed deep on one side, then on the other side, of the penis. Lastly, what remains in the syringe is injected into the under side of the penis. The urethra and dorsal vein should be avoided if possible. The most important point is to wait fifteen minutes after making the injection before beginning to operate. Patients will often detect a pinprick after acute sensation is lost, but do not feel the cut of the scissors or the burn of the cautery if one is careful to postpone work for the period mentioned. Miller (Jour. Amer. Med. Assoc., May 7, 1910).

Conduction anesthesia is available for any size of nerve. In the case of the larger trunks, an injection is made directly under the nerve-sheath (intraneural method). Large nerves are, however, usually deeply ensconced in the tissues; hence preliminary superficial analgesia is generally required before they can be reached. In **amputations** the large nerves supplying the part are frequently "blocked" expressly for the purpose of avoiding the shock resulting from their division.

After injection of cocaine into a nerve it is still painful when taut, but not painful when relaxed. The periosteum could be incised without pain, in an **amputation for senile gangrene**, for example, after local injection of 1.5 c.c. (24 minims) of 0.5 per cent. cocaine. The sawing of the femur caused no pain, nor the curetting of the bone-marrow for 1.5 cm. above the cut surface. Dry gauze was then applied to lessen the absorption of cocaine. Another patient had his arm amputated without

pain after the inflamed periosteum had been injected with a 0.25 per cent. cocaine solution and turned back from the bone. Lennander (Deut. Zeit. f. Chir., Bd. lxxiii, Nu. 4-6, 1904).

The secret of success in ordinary local anesthesia for large operations lies in waiting for fifteen minutes at least before commencing. Braun's subcutaneous perineural injection on the nerve leading to a hernia has supplanted Cushing's method. The "twilight sleep" is sometimes useful as a preliminary to local anesthesia, especially for excited patients with exophthalmic goiter. Bier (Archiv f. klin. Chir., Bd. xc, Nu. 3, 1909).

Local anesthetization of the pudic nerve, as suggested by Ilmer, found very satisfactory, enabling suture of **tears in the perineum**, application of forceps and extraction of the fetus, even in primiparæ, without pain, besides various gynecologic operations. A considerable amount of anesthetic fluid is injected around the nerve (n. pudendus) in different directions and at various depths, thus encircling the nerve and its branches near the ischiorectal fossa. The spine of the ischium is inside of the great sacro-sciatic foramen, through which the nerve emerges, and is useful in locating it; the injection is best made along the stretch of the nerve between the ischiorectal fossa and the lesser sacrosciatic foramen. The point of injection is readily marked with the thumb of the palpating hand, to the side of the anus, about the middle of the inward slope of the tuberosity of the ischium, while the middle finger in the vagina locates the spine and the index finger controls the progress of the needle. The control can also be made by a finger in the rectum. H. Sellheim (Zentralbl. f. Gynäk., July 2, 1910).

Technique for **amputation of breast** under local anesthesia described. The field of operation is outlined with a series of ten injections, pointing the needle in four directions to

spread the fluid. The first puncture in the axilla is the only one that is painful, the others being all at previously anesthetized points. G. Hirschel (Münch. med. Woch., March 7, 1911).

Two cases operated successfully on the elbow and ulna for the removal of fractured bones, and a third case for tuberculous osteomyelitis, under local anesthesia of the brachial plexus, in which the anesthetic was directly injected into the plexus. Hirschel (Münch. med. Woch., July 18, 1911).

There are certain operations in which a general anesthetic is distinctly contraindicated, regardless of the heart and kidneys. One is in **pleural empyema**; here a general anesthetic is given in nearly all cases, and much damage is usually done by the uncontrollable coughing as the patient is recovering from the anesthetic. With local anesthesia this can be obviated.

The technique is as follows: Locate the point of entrance, usually the eighth rib in the axillary line; make a wheal upon this rib at each end of the proposed incision, and inject the interspaces above and below; wait about ten minutes, and cut down to the periosteum. Now take a curved needle and slip it under the lower border of the rib and inject into or close around the nerve itself, and into the space between the rib and the parietal pleura. Wait ten minutes for this to take effect. Then incise the periosteum along the middle of the rib and raise it up on both its surfaces with appropriate periosteotomes. Place the rib-cutting forceps as usual and remove the entire rib for one and a half inches. One can now open into the pleura at once and either drain it rapidly or more slowly with a syringe or needle. O. S. Fowler (Denver Med. Times, Jan., 1913).

*Schleich's infiltration anesthesia* consists of the production of an artificial edema by the injection of a consider-

able amount of a very dilute solution of cocaine or other analgesic, and was employed by its originator in all kinds of operations, including laparotomy. Three solutions differing in strength were recommended by him, of which that generally used consists of 1:1000 cocaine hydrochloride and 1:4000 morphine hydrochloride in 0.2 per cent. sterilized sodium chloride solution, together with 1:12,000 phenol as preservative.

In carrying out the infiltration, a small area on the skin near the field of operation is sprayed with ethyl chloride, and, when it is insensitive to pain, cocaine solution is injected intradermally with a long and very fine hypodermic needle held almost parallel to the skin. At this point a wheal or lump at once arises, which may be made as much as one-half inch in diameter, and which is absolutely without sensation. The point of the needle is now pushed farther under the skin through the area of insensibility and a few drops again injected. Another wheal rises close to the first. By extending these injections farther and farther round the field of operation, reinserting the needle only after its entire length has passed under the surface, the whole area is infiltrated. The anesthesia is immediate and generally lasts about one-half hour. (O. S. Fowler states, however, that by forming a double row of wheals, and incising between them, the skin will remain well anesthetized for an hour or longer.) The injections must always be made into healthy skin; otherwise, sloughing may follow. The subcutaneous tissues, fascia, and tissues still deeper in are similarly infiltrated.

Some surgeons infiltrate from be-

low upward—i.e., the skin last—where the tissue layers are thick, as the extensive edema otherwise renders correct infiltration of the deeper tissues difficult.

Where extensive **gynecologic plastic operations** are to be done, or where these may be followed by abdominal work, the Schleich solution No. 2 may be advantageously employed, a small amount of formalin being added to lessen the risk of infection. The author performed various plastic operations on the vulva, cervix, and vagina, and also extirpated the diseased uterus and adnexa through the vagina under this form of anesthesia. The abdominal operations which were done included the **removal of tubes and ovaries, shortening the round ligaments, myomectomy, hysterectomy, appendectomy, and resection of the intestine.** A strong suggestive influence is obtained by sprinkling a few drops of chloroform on a mask held over the face. In extreme anemia and sepsis, the local anesthesia greatly diminishes the risk, as in a case of **ruptured ectopic gestation** where the hemoglobin was less than 24 per cent. J. C. Webster (Jour. Amer. Med. Assoc., April 23, 1904).

The sense of pain is present in normal abdominal organs, and is considerably augmented in inflamed organs; a subcutaneous or intramuscular injection of cocaine is capable of completely abolishing this sensation in normal as well as in inflamed organs. Kast and Meltzer (Med. Record, Dec. 29, 1906).

Infiltration anesthesia employed with success in **gastrostomy, herniotomy, suprapubic cystotomy, closure of an artificial anus, laparotomy for intestinal obstruction, radical cure of varicocele, removal of a mass of suppurating tuberculous glands** in the groin, extirpation of the saphenous vein and its tributaries for **varix.** Arnold (Brit. Med. Jour., March 23, 1907).

The anesthesia produced by Schleich's method is due not only to the cocaine injected, but to the pressure exerted by the fluid on the sensory nerve-endings and filaments, the function of which is thereby abolished. The amount of cocaine required to produce analgesia of a given area is thus decreased; for small areas the total amount of cocaine used can be diminished and the risk of toxic effects likewise, while if the full amount of cocaine permissible be employed larger areas can be anesthetized than would otherwise be the case. One hundred cubic centimeters of the solution already referred to can be injected without danger (Hildebrandt), for part of the fluid escapes when the solution is made, while the rest is only slowly absorbed. For extensive operations Schleich advised a solution containing only 1:10,000 of cocaine; where acute inflammation is present, on the other hand, a 1:500 solution is to be employed.

The discovery of new analgesics of lower toxicity than cocaine, as well as the knowledge of the fact that the fluid injected should be isotonic with the body fluids if pain during injection and injury to the tissues are to be completely avoided (Braun), have led to the use of solutions other than those of Schleich. Thus, Barker has advised a fluid consisting of beta-eucaine, 3 grains (0.2 Gm.); sodium chloride, 12 grains (0.8 Gm.), and distilled water,  $3\frac{1}{2}$  fluidounces (100 c.c.), to which is added, after boiling, 10 minims (0.6 c.c.) of 1:1000 epinephrin solution. Pels-Leusden uses sterile tablets each containing 2 grains (0.125 Gm.) of novocaine and  $\frac{1}{884}$  grain (0.00016 Gm.) of boric epi-



satisfactorily by introducing the eucaine solution near the web so as to act on the nerve trunks. In the former operation it need only be injected into one side, but in the latter it is necessary to inject both sides of the toe. A comparatively large quantity should be used, and the operation not commenced for at least twenty minutes. Porter (Jour. of the Royal Army Med. Corps, March, 1908).

Local anesthesia by the infiltration method is the best for plastic **operations on the perineum and vagina**. Epinephrin should be used only in the smallest amounts and weakest concentration in operations on the female genitals. Lobinsky (Zentralbl. f. Gynäk., Dec. 10, 1910).

Schleich's method presents disadvantages in that the infiltration of the tissues may render the recognition of the structures to be dissected difficult, and that it produces intense pain when practised in tissues the seat of inflammation.

The operations especially well suited to Schleich's local anesthesia are: the extirpation of **benign encapsulated tumors, resection of ribs**, typical operations on the abdomen, such as **gastrostomy**, etc., where one has not to search too much inside the peritoneum, as pulling on the mesentery and omentum causes both great pain and much shock. It is not well adapted for the removal of **malignant tumors** and operations on inflamed areas. Hildebrandt (Berl. klin. Woch., May 1, 1905).

Local anesthesia by the infiltration method used in over 200 cases without bad effects. The cases include **herniotomies, varicoceles, hydroceles, resecting of ribs, exploratory incisions of abdomen, appendectomy**, external clamp on **fractured bones, nerve anastomoses, suprapubic cystotomies, orchidectomies, amputations, skin grafting** by the Thiersch method and with whole thickness of skin, wiring of **fractured patellæ**, removal of large

**lipomata, circumcisions, plastic operation on penis**. Large portions of omentum were resected during **hernial operations**, and local anesthesia used for the **removal of various foreign bodies** and repair of numerous **accident wounds**. Local anesthesia may in a great measure replace general anesthetics, thereby increasing the safety of the patients, without in the least adding to difficulties. O. S. Fowler (Denver Med. Times, Jan., 1913).

(c) **Cataphoresis**.—The induction of surface anesthesia by the passage of a galvanic current through the part, the positive electrode consisting of a piece of gauze or blotting paper moistened with cocaine solution, has been advocated by some authors, notably H. Lewis Jones, who employed a solution consisting of 6 grains (0.4 Gm.) of alkaloidal cocaine in 1 dram (4 c.c.) of guaiacol. Tousey doubts, however, that the local effect of this mixture is any greater than that which would result from the application of guaiacol alone.

Cocaine cataphoresis used for removal of **tumors of breast**, removal of **lip for cancer**, and in operations for **hernia, hemorrhoids, birthmarks, moles**, and **epithelioma**. A piece of gauze folded four times is cut the size of the part to be anesthetized and laid on the skin, previously made sterile. The gauze is then saturated with the following solution:—

℞ Cocaine hydrochloride ..... ʒiiss (6 Gm.).  
Epinephrin solution . ʒij (8 Gm.).  
Sterile water . q. s. ad ʒij (60 Gm.).

The gauze is next covered with metal foil connected with the positive pole of an electric battery. The circuit may be completed by the patient holding in his hands a wet sponge electrode connected with the negative pole, or a large pad electrode may be used as the negative pole and

attached by a bandage to the skin near the part to be operated on. The time required for anesthesia is fifteen to thirty minutes, and may be longer for deep effects. No bad effects ever observed from the method. D. T. Quigley (Jour. Amer. Med. Assoc., Feb. 23, 1907).

(d) **Intravascular Injection.**—*Intravenous anesthesia* was introduced by Bier in 1908, and consists in the injection, after exsanguination and ligation of the member to be operated on, of from 40 to 150 c.c. ( $1\frac{1}{3}$  to 5 ounces) of 0.5 per cent. novocaine in normal saline solution into a superficial vein. Since cocaine is not used in this form of anesthesia, the method may be more properly discussed under Novocaine, to which the reader is referred.

The unsuitability of cocaine introduced intravenously for the production of general surface anesthesia without loss of consciousness in man was definitely shown in 1911 by Harrison, through experiments performed upon his own person.

Report of observations made by the author on himself with the intravenous use of cocaine. Into a superficial vein on the back of the hand were introduced 5 grains (0.32 Gm.) of cocaine in a 2 per cent. solution in the course of about thirty minutes. Cerebration was normal except for an inability to keep the mind long on one subject. Motor power was unimpaired. There was marked analgesia everywhere. An incision three-fourths inch long through the skin, well down into the fat, was made on the anterior surface of the lower leg. The incision could be felt, though causing a mere trifle of pain. The relatively enormous dose necessary for even such an imperfect result makes the method quite impossible for human surgery. Harrison (Boston Med. and Surg. Jour., Feb. 2, 1911).

*Intra-arterial anesthesia*, advocated by Oppel and Ransohoff, consists essentially in the injection of the analgesic drug—cocaine only has as yet been employed in this method—into an artery *with the blood-stream*, and is in other respects carried out in the same manner as Bier's intravenous procedure.

As shown by the observations of Oppel, the fatal dose of cocaine is eight or ten times as large when the drug is injected into an artery as when it is introduced into a vein, owing to the broad area of vascular ramification, through which it is necessarily exposed to oxidizing influences before returning to the vital structures. This fact, however, bears but little on the relative safety of the intra-arterial and intravenous methods, since interruption of the circulation in the part operated upon is practised in each. So far the intravenous method has found more favor than the intra-arterial.

Anesthesia may be induced by the injection of cocaine solution directly into the artery supplying the area to be anesthetized. Very little, if any, is returned through the veins to the general circulation. The following technique is recommended: The main artery supplying the part to be anesthetized is exposed under infiltration anesthesia. An Esmarch bandage is bound about the limb some distance above the point of proposed injection. The tourniquet should be snug enough to constrict the veins, but not so tight as to interfere with the arterial circulation. From 4 to 8 c.c. (64 to 128 minims) of 0.5 per cent. cocaine in normal salt solution are then injected into the artery in the direction of the blood-stream. The needle should be as fine as possible. After anesthesia is complete, the Esmarch bandage is removed and the wound closed. The

maximum dose suggested contains only 0.04 Gm. cocaine, a safe dose.

The method is particularly applicable to the upper extremity, where the brachial, radial, or ulnar artery may be exposed with little difficulty. For the larger operation on the lower extremity when general anesthesia is contraindicated, spinal anesthesia seems more desirable. For operations about the foot and ankle the method also has a distinct place. Ransohoff (Ann. of Surg., Apr., 1910).

(e) **Spinal anesthesia**, produced by the injection of an analgesic agent into the spinal subarachnoidal space, generally in the lumbar region, will be dealt with in a special section. (See Spinal Anesthesia.)

## COCAINOMANIA, OR COCAINE HABIT.

**DEFINITION.**—Cocainomania is an irresistible craze, crave, or impulse to intoxication by cocaine, or any of its salts or combinations, at all risks. Unless a cure of the "habit," or, more accurately, the disease, of cocainomania be effected, the cocaine habitué cannot refrain from resorting to the employment of the drug, if a supply can possibly be procured, whenever the craze, crave, or impulse seizes upon him (Kerr).

**VARIETIES.**—The two leading types of the cocaine habit are: (1) *periodical*; (2) *continuous*. In the former the habitué will, after an outbreak of cocaine intoxication, go on without cocaine in any form for a longer or shorter interval, till a condition of mental unrest, arising sometimes apparently from within, ushers in a period of more or less complete temporary abandonment to the drug. Sometimes the outburst is inaugurated by a recurrence of the acute pain, or the asthma, or other physical

trouble, for the assuagement of which the poison was originally taken. In some highly strung women the menses act as the exciting provocative, particularly when accompanied by acute dysmenorrhea. In the latter variety, the continuous, the unfortunate victim keeps on steadily taking the drug daily in rapidly increasing quantities till he or she is rendered incapable of exertion, sometimes of connected thought, by advancing paralysis or by insanity. In some instances the indulgence is *social*, in others *solitary*, the latter being the rule and the former the exception.

In large cities, until recently alcohol, morphine, ether, and a few other agents predominated as psychic intoxicants; at present cocaine leads them all, owing, it is believed, to the ease with which it may be taken,—no syringe, no painful needle pricks, no marks on the arms, etc.,—while the pleasurable sensations sought are obtained without a relatively prolonged stage of habituation. Briefly, a mere snuff containing cocaine in suitable quantities suffices for all purposes. This class of cocaine habitués may be readily recognized by their frequent sniffing, their tremors, and the habit of "bug-hunting" in the skin of their hands and arms in obedience to abnormal sensations or paresthesias caused by the drug. Hallucinations, phantoms, and a sort of delirium of persecution complicate marked cases and render the victims querulous and frequent visitors to the police stations. A curious symptom is a predilection for rapid progression; the automobile is a boon to these patients, unless, as frequently happens, they overlook the cost—another cause of trouble with the police, leading often to incarceration in an insane asylum. The nasal cavities sooner or later show a characteristic lesion: necrosis of the septum due to the denutrition caused by the constricting action cocaine has on



the local arterioles. André Lanthéaume (*Revue de thérap.*; N. Y. Med. Jour., Jan. 25, 1913).

The constant use of cocaine upon a mucous membrane produces congestion and tumefaction, followed by atrophy and anemia; but the sensibility of the mucous membranes is not affected. Catarrhal affections are less prevalent than in non-users of the drugs. Heroin produces a thin, acrid discharge, and cocaine causes epistaxis. Ridpath (*Laryngoscope*, Jan., 1916).

A number of cases of serious inflammation of the eyes after operations in which cocaine solutions had been used as an anesthetic, are reported by the writer. He attributes this inflammation to the solutions not being completely sterile and advises not to keep any stock solutions of cocaine hydrochloride and to use freshly made solutions boiled for three minutes immediately before use. Tyndalizing does not render the solutions sterile and heating for any length of time at a higher temperature produces decomposition of the alkaloid. Baumeister (*Klin. Monatsbl. f. Augenheilkunde*; Amer. Med., Dec., 1917).

Necrotic ulceration of the septum is common among those who snuff cocaine. It develops within 2 or 3 months, and often results in perforation. This is liable to be attributed to lues if the addiction is not known, and recruits have been rejected on this account alone, the history of the cases not being brought out clearly enough to explain matters. Turtur (*Policlinico*, May 5, 1918).

Some variation is observable when cocaine addiction is associated with alcoholic or other narcotic indulgence. In this way the addiction may be double, triple, or fourfold: twofold, as alcohol or morphine with cocaine; threefold, as with alcohol and chloral; fourfold, as with alcohol, morphine, and chloral.

**SYMPTOMS.**—On taking a fresh dose, in chronic cocainomania, there

are, generally within ten minutes, exuberance of spirits, quickened pulse, general acceleration of the circulation, talkativeness, restlessness, hallucinations, with rapid and somewhat spasmodic breathing, intense joyous activity, and a remarkable overconfidence in one's capacities and strength. Even when actually weaker, during the cocaine-delirious intoxication, the taker feels infinitely stronger and more agile. Occasionally there is vertigo, with some confusion of the intellectual faculties. There is usually great cerebral excitement, with dilated pupils, throat dryness, and headache, the last-named frequently not severe enough to be painful. There is a rise of temperature, with a loss of the sense of time, though memory is usually intact. Depression and prostration follow very often. When the dose has been relatively moderate,—i.e., not larger than the cocaine-taker has been gradually accustomed to take,—the period of nervous hyperexcitation has passed away by from half an hour to two hours. When the dose taken has been relatively immoderate, the depression and nervous debility may remain for days or till the next dose.

In chronic cocaine poisoning, though some habitual cocainists do not appear to show any symptoms of injured health or vigor, others appear wasted, with pale-yellowish skin, the extremities clammy, with cold perspiration. The eyes are glistening and sunken, with dark, subocular rings, the pupils being dilated. Anorexia and impaired digestion are present, with palpitation, dyspnea, tinnitus aurium, tremors, neurasthenia, and uncertainty of step. Hallucinations, especially of sight and

hearing; mistrust; delusions of persecution, and general paralysis sometimes end the scene. Yet, in some cases, one sees occasional spells of brightness, brilliance, and mental activity (Kerr).

The needle punctures in chronic cocaine poisoning leave traces of brown, almost black, pigmentation; this is a sign peculiar to cocaine. The paresthesias are not located at the periphery, but on the trunk, and they produce the subjective impressions of foreign bodies under the skin. Most characteristic of all is the delirium with hallucinations; it resembles the alcoholic delirium, but there are no objective signs of liquor drinking. The patient during the delirium can reason logically and behave normally in regard to surrounding objects until unconsciousness supervenes, the condition thus differing from that of ordinary drunkenness. There is at first an exalted self-consciousness, followed by dyspnea and distress. The hallucinations may drive the patient to commit suicide,—an extremely rare occurrence in alcoholic delirium, even the most aggressive. Cocaine can be suppressed abruptly. Higier (Münch. med. Woch., March 7, 1911).

### DIFFERENTIAL DIAGNOSIS.

—Though, in many cases, unless the presence of cocaine can be determined by finding the drug or by the brown stain over the seats of hypodermic injection, this particular "habit" or mania cannot be diagnosed from other forms of narcotic addiction, there are one or two prominent symptoms which point to cocaine as the special mania. Especially in the earlier stages, though to a larger extent in the more advanced, alcohol is excluded by the absence of symptoms pointing to organic functional bodily lesion.

The cocainomaniac not only quite

often shows no symptom of bodily or mental disturbance, but manifests simply a sense of satisfaction, and an appearance of increased capacity for intellectual and muscular work. In many cases the closest physical examination has failed to reveal anything abnormal. Indeed, at times the only symptom discernible has been an apparently improved condition.

An important aid in diagnosis is a knowledge of the method employed in taking cocaine. Of the total 23 cases studied by the writer 21 snuffed up the drug. In only 2 instances was the hypodermic needle used. In the 8 cases of acute cocainism, observed in old habitués who had taken more than their usual amount, the following symptoms were presented: The pulse rate was increased, ranging between 82 and 120; the respiration was varied, occasionally slow and prolonged, more often rapid, irregular, or sighing; the body heat was increased, the highest being 102.4° F. (39.1° C.); the body and extremities were occasionally convulsed or spasmodically twitching, sometimes tetaniform; emotional excitement and inco-ordination were frequent; hallucinations were, not rare, including those of sight and common sensation, association with delusions of persecution, suspicion, and jealousy. The classical sign of a feeling of vermin crawling over the body was observed but once. Following a cocaine debauch, temporary insanity may result, and 2 such cases were observed. Restlessness, insomnia, anorexia, and hallucinations were common to both. The after-effects of acute cocaine poisoning are pallor and anemia, not infrequently tremor. The eyes are sunken and have a nervous, wandering expression. The symptoms of chronic cocaine poisoning are fairly definite, including dyspepsia, loss of weight, anorexia, and a peculiar inability to concentrate the mind; but these are not especially diagnostic, as they occur in

other drug habits. The writer calls special attention to intranasal ulceration on the septum as a diagnostic symptom. The detection of 14 of the habitués in this series depended on this sign, and he knows of 6 additional cases thus detected. W. D. Owens (Jour. Amer. Med. Assoc., Feb. 3, 1912).

In some instances only the closest continuous scrutiny of a business partner or a wife has, after a time, disclosed even the slight falling off in the character of the work and of the judgment, the actual amount of work having been occasionally increased.

**Etheromania.**—One point of differentiation, even from this state (which is more speedy in the appearance, progress, and cessation of toxic symptoms than either alcohol, opium, morphine, chloral, or chloroform), is the greater quickness with which the characteristic phenomena of cocaine poisoning set in and pass away. Still another discriminating symptom is the extraordinary self-confidence and elation arising from cocaine. In etheromania the odor of the breath is characteristic, and the activity more effervescent and demonstrative.

**Alcoholism.**—A point of distinction from this habit is that, while this is mostly social and much less often solitary, cocaineomania is almost always solitary. Yet another difference from alcohol and morphine is that the prevailing delusions of cocaineomania are delusions of persecution. These rarely occur with alcohol, except temporarily sometimes in delirium tremens or in chronic alcoholism, and still less often with morphinomania. They are frequently seen, however, with the chronic co-

caine habit, and are at once more marked and more persistent with cocaine.

The subject of alcoholomania shows greater evidence of morbid change; the subjective and objective symptoms are more marked. There is distinct attraction for social pleasures, whereas the narcomaniac prefers solitude.

There is a strong resemblance between cocaineism and alcoholism. **Morphine** is of value in either case. The cocaine psychosis is an acute hallucinatory insanity, with a greater tendency to suicide than is shown by the alcoholic. Cocainomania is easily curable and but seldom relapses. Withdrawal does not occasion the severe abstinence phenomena present in alcohol and morphine habitués. Higier (Münc. med. Woch., March 7, 1911).

**Morphinomania.**—Characteristic symptoms set in and disappear much more quickly than in morphinomania. Cocainomania is characterized by marked self-confidence and elation (Norman Kerr).

**ETIOLOGY.**—On the nervosanguine and passionate temperaments cocaine has a special excitant power. Once taken in any form for the assuaging of acute pain, on such temperaments this drug fastens as if with a grip of iron imbedded in velvet. In one case of a life-abstainer from alcohol, cocaine, taken once during a prostrating attack of agonizing pain, exercised so powerful a hold that only after a strenuous struggle of over a week's duration could the veteran nephelist overcome the imperious impulse to take a second dose. He felt that, if he yielded, his will would have been rendered powerless for the future against the tremendous fascination of

the drug which had banished his pain as if by magic, and of the name and other properties of which he was utterly ignorant. In "neurotics" a few doses, taken medicinally, suffice to set up the "cocaine habit." In transmitted gout, with irritable and susceptible brain and nervous system, this special predisposition has been markedly present. It has also been noted in syphilis and scrofula with cerebral complication. Epileptic neuroses have been greatly in evidence.

Cocainism is the most insidious of all drug habits. The use of the drug being unaccompanied by disagreeable after-effects,—headache, nausea, vomiting, etc., which are met with after the ingestion of opium or alcohol,—the vice is readily and rapidly established. It is occasionally acquired by the local use of the drug in diseases of the nose and throat, teeth, etc., but more often as a substitute for opium or alcohol.

Cocaine is eventually tolerated by the system in huge doses. One case is recorded where 60 grains (4 Gm.) were daily consumed. A relatively large number of habitués are found in the medical and dental professions (it is said 30 per cent.). The continued indulgence in cocaine invariably, and usually soon, leads to marasmus, with mental, moral, and nervous degeneration. The smallest fatal dose on record is  $\frac{1}{8}$  grain (0.021 Gm.) hypodermically. G. W. Norris (Phila. Med. Jour., Feb. 9, 1901).

Series of 15 cases in which the habit had been acquired by men employed where the drug was manufactured. The ages of the men ranged from 23 to 40 years, and the daily quantity taken, from 20 to 60 grains (1.3 to 4 Gm.). The method of taking was solely by snuffing, it probably being the most convenient and most easily managed. C. G. Steinmetz, Jr. (Jour. Amer. Med. Assoc., Apr. 10, 1915).

Over and above the psychological excitation of the drug itself, the exciting causes seen by Kerr have practically been confined to urgent clamor for relief from physical agony, such as occurs at times in asthma or neuralgia. One of its most frequent causes is the therapeutic use of snuff containing cocaine. But it is also used in this form to incite pleasurable intoxication, as is the case with alcohol. At the present writing (1913) this form of intoxication is common in Paris, according to Lanthéaume, Briand and Vinchon.

Insomnia does not incite to cocaineomania as it frequently does to morphinomania. Physical pain has been the initial starting point. The use, for any purpose, of cocaine is an unmistakable influence inciting to the "cocaine habit" in constitutions predisposed to narcotic excitation. Other narcotic substances also both predispose and excite to the cocaine mania. Morphine, for example, long continued is apt to create a crave or impulse too imperious to be satisfied with morphine narcotism alone.

In morphinomaniacs cocaine is sometimes resorted to simply with the object of heightening the pleasurable sensations of intoxication. In not a few instances cocaine addiction has been rapidly set up in the vain attempt to cure alcoholomania or morphinomania by substituting cocaine. This attempt at the cure of the original form of narcomania (a mania for narcotism by any narcotic) is sometimes openly attempted with the best intentions; but is more often unknowingly tried simply because cocaine has been a component of the so-called "cure," though not disclosed by the manufacturers. In this way

even some abstainers from alcoholic liquors who pride themselves on their consistent temperance have insensibly become cocaine slaves, they having had no idea that they and theirs were partaking of a narcotic poison more fascinating and perilous than the object of their aversion: alcoholic intoxicants. A striking object lesson of medical unwisdom was the appearance of a crop of cocainomaniacs in England shortly after the announcement, in a British medical annual, of the reputed cure of alcoholomania and morphinomania by means of cocaine, in another country.

Below 16 years of age there would appear to be a lessened susceptibility as the years go down, children showing less cocainomaniacal proclivities than adults, and not responding so readily to the narcotic properties of the drug in doses relatively corresponding to their years. Though the young are readily intoxicated by cocaine, they are not so prone to become subject to the mania for intoxication by cocaine.

As to sex, the majority of the cases have been male; but this has not arisen because of a lesser susceptibility that is found in man, but probably is owed to occupation exercising a stronger influence.

Occupation is a predominant factor, most of the victims having been medical men, members of the legal profession, literary men and women, and the cultured generally.

Climate exercises considerable influence, which may account for the greater prevalence of cocainomania in the United States of America, and northern France, as compared to Great Britain. Racial characteristics and atmospheric conditions modify

purely climatic environment, however; witness the practical absence of cocainomania among the great community of the Jews, and the rapid electrical disturbances, as well as the tremendous temperature alterations, of North America.

The cocaine inheritance has not had time to show itself, if it exist; but the "cocaine habit" as an outcome of transformed narcomaniac transmission has been noted by Kerr.

**PATHOLOGY.—Acute Cocainism.**—Though a large number of cases of acute cocaine poisoning have been recorded by Germain Sée, Mattison, Schede, and others, comparatively few have proved fatal. Probably the fatalities have run not much over 10 per cent. Even in exceedingly grave cases, when the sufferer appears almost moribund, the distress and collapse often suddenly and unexpectedly give way and the apparently dying patient makes a good recovery. Hence there has been little opportunity for post-mortem inspection. Clifford Allbutt says that the heart is found in diastole and the nervous centers are congested. According to Ehrlich, vacuolar degeneration is found in the hepatic cells, the latter being greatly enlarged and the nuclei atrophied. The convulsive respiratory paralysis is ascribed by Mosso to tetanus of the respiratory muscles, and the great rapidity of the circulation to paralysis of the vagus. The peripheral blood-vessels are contracted. Cocaine is stated to alter and injure the leucocytes; Maurel and Beaumont Small state that these become spherical and rigid, with increase of size. They seem also to have a tendency to locate next to the vessel wall.

Death may supervene at an early stage from syncope, or at a later from asphyxia. Cocaine acts on the central nervous system and also upon the circulatory apparatus. Doubts have been expressed as to whether the anesthesia produced by cocaine is due to the vasomotor disturbance or whether the drug directly paralyzed the nerve-terminations. Brown-Séquard believed the latter, holding that cocaine acts through the peripheral nerves on the nerve-centers, which react in inhibiting sensibility. As shown in the section on Cocaine in the present article, it causes primary central excitation followed by depression.

**Chronic Cocainism, Including the Mania for Cocaine.**—A distinction ought to be made between the physical poisoning by the drug (cocainism) and the overpowering mania for the drug (cocainomania, or the "cocaine habit"). Of the pathology of the latter little can be said specifically. Altered scavenger or spider-cells are found in the brain; but as most cocaine habitués have previously been indulgers in alcohol, no reliance can as yet be placed on these appearances as pathognomonic of cocaine mania. Marasmus, with absence of fat, is usually the most prominent after-death appearance, and there has not been noted the darkish hue of the stomach's interior which has been seen in some cases of fatal opiomania. The post-mortem appearances include dark and fluid blood, with congestion of lungs and other organs, but these are not peculiar to cocaine poisoning. There have not been observed traces of cocaine tissue degradation and organic degradation which are so often met with in the stomach, liver, kid-

neys, and other vital organs of alcoholic cases, unless when chronic alcohol poisoning has preceded or accompanied the cocaine indulgence. When cocaine is contemporaneous with chronic morphine poisoning the wasting is even more marked. Though the minimum fatal dose in acute cocaine poisoning is not quite fixed, death has been recorded as the result of less than half a grain, and several deaths have occurred after 8 to 12 grains; yet the habitué can set up such a tolerance of the drug as to raise the daily consumption to some 30 or 40 grains. In some instances the daily average has been more than double this. In 1 case 80 grains a day were subcutaneously injected, besides 60 grains of morphine. One death occurred in twenty minutes, one in four minutes, and a third in forty seconds (Hamilton and Godwin).

**PROGNOSIS.**—The prognosis of *acute* cocaine poisoning is, on the whole, favorable. Even though death almost always seems impending from the gravity of the symptoms, the great majority of cases recover if judiciously treated soon after the poisonous dose has been taken. Generally, after three-fourths hour the prognosis is even more favorable. This cannot so unreservedly be said of *chronic* cocaine poisoning (the cocaine habit, or cocainomania), of which the outlook is, under ordinary conditions, unfavorable. If, however, the patient surrender his liberty and place himself absolutely under control in a special home or in a hospital for a sufficiently long period, the prognosis may fairly be considered to be more favorable. The prognosis of cocainomania is not nearly so

favorable as that of alcoholomania or even morphinomania. Cocaine exhausts the mental capacity more rapidly than either morphine or alcohol; it takes a greater hold on the brain and nervous system, reducing his intelligence and benumbing his faculties, setting up a moral palsy which seems to annihilate inhibition and to deprive the victim of all desire for deliverance. There are, however, exceptional cases which exhibit a strong wish to be cured, which are hopeful and have been delivered under treatment at home (Kerr).

**TREATMENT.**—In the treatment of the cocaine habit, or chronic cocaine intoxication, it is more essential to have **complete control** of the cocaineomaniac and his actions than even in chronic alcohol or morphine mania. There is less influence to be borne in the brain- and nerve- centers of the chronic cocaineist than in those of the chronic alcoholic or chronic morphinist. There is less mental and moral elasticity, less desire to be freed from the narcotic bondage, less consciousness of the bondage itself, a more helpless and hopeless wreck being difficult to find. Cocainomaniacs, however, are, in a few cases, cured without seclusion. In these hopeful cases there generally has been a greater stock of inhibition from the first. Again, the indulgence having been periodical and ordinarily provoked only by some recurrent neurotic pain or distress, and leaving intervals of shorter or longer non-narcotic consumption between, inhibition has not been so paralyzed, and thus there has been more resisting power left. In the latter group of cases it is imperative to direct the treatment and all auxiliary measures

to the abolition or counteraction of the exciting influences.

In the mass of cases the main hope of cure rests in **therapeutic seclusion**. The patient must be treated as a diseased person. **Diet**, at first simple and readily assimilable, should be carefully attended to. Milk, with soda or lime water and **effervescent**s if nausea and emesis are present; arrowroot or other farinaceous or malted food, and other peptonized preparations are excellent. Gradually, broths and plain soups, oysters, fish, poultry, and, lastly, mutton, and red meat, with an ample supply of fruit and vegetables, may be given. But there are cases in which a non-fish-and-flesh dietary agrees better with the patient. Each case must be carefully observed to determine the most suitable dietetic instructions.

In the first week **exercise** and **fresh air** may usually be insisted on, with **massage** to improve the wasted condition of the muscles. Meals should be regular, and exercise graduated.

Alcoholic beverages are best avoided; and though in a few cases tobacco in limited quantities may be allowed to aid in staying the morbid impulse or crave, most cocaineomaniacs would be better without it in any form. Tobacco is apt, in many patients, to impair digestion and depress the heart's action, the healthy state of both vital processes being points of the highest importance in the treatment of this mania.

To combat the wearing insomnia of most cases the **hot, wet pack** is very useful. Of all the medicinal hypnotics, **phenacetin** is the most useful, in doses of 5 grains, repeated, if necessary, every hour; no more than three doses (15 grains) to be

taken in one night. Others have found **chloral**, **trional**, and **sulphonal** serviceable. It must not be forgotten, however, that all these hypnotics tend to depress, and that in advanced cases they may retard recovery. They should therefore be used with care.

An important practical point is the method of **complete withdrawal of the cocaine**. This complete withdrawal is essential to cure, and should invariably be resorted to where practicable. Where it is not, the reduction period may be spread over from seven to nine days, beginning, whatever the quantity which had been taken daily or how long, with a reduction of one-half. Welch Branthwaite has repeatedly stopped the cocaine, after giving but one dose, without trouble. These were cases in which morphine had also been freely used. Where morphine is also freely and regularly taken, it is easier to withhold the cocaine without delay.

Chronic patients may be treated by stopping the drug at once, by rapidly reducing it, or it may be slowly withdrawn. In many cases its immediate withdrawal will be the most satisfactory, for the reason that during the gradual reduction it sometimes happens that the patient will not remain under treatment when the discomfort incident to the partial deprivation manifests itself strongly; in other states where institutional detention is lawful, these patients are more easily managed by confinement. When maniacal symptoms are present, they usually subside when the individual can no longer obtain the poison. The suffering attendant upon deprivation is not so great as in the morphinist, but there is danger of the symptoms of collapse for some time after the drug has been withdrawn. **Strychnine** is a sustaining remedy;

the mental distress may be relieved by **hyoscyamus**, **valerian**, or large doses of **bromide**; the appearance of collapse should be met by the administration of **cardiac and respiratory stimulants**; the insomnia is best overcome by **prolonged baths**; **good food** should be given at frequent intervals. N. S. Yawger (N. Y. Med. Jour., Dec. 3, 1910).

After a description of the symptoms of the habit, among which is mentioned perforation of the nasal septum, which is becoming recognized as characteristic, the writers state that some 50 per cent. of the women of the street snuff cocaine. Most of them begin by using the drug secretly, but soon become reckless and snuff it in more or less public places without shame. The ease with which the drug is taken makes victims much more speedily than alcohol, morphine, or the once-popular ether, but there are many victims of various combinations of the narcotics. Cocaine takes such a hold on women that they sell their furniture, furs, and jewels at ridiculously low prices to obtain it. The Apache, or gunman, and the sexual invert are also cocainists, as a rule. France has severe laws against the sale of narcotic drugs, but so far their effect has been, in Paris as well as nearer home, simply to raise the price, often at late hours of the night to four dollars a dram. Marcel Briand and Vinchon (*Semaine médicale*, Jan. 8, 1913).

All complications must be attacked, but, in the main, besides hygienic measures, **nervine tonics** are indicated in the endeavor to restore the lost energy and will-power which really constitute the disease. Of these tonics **nux vomica** and **strychnine** are the most effectual. **Arsenic** also is useful. It has been found in this, as in other narcomanias, that an occasional replacement of the stronger nerve tonics by milder ones is advantageous—agents such as **quinine**, **ca-**



**lumba, and gentian. Galvanism** has, in appropriate cases, its value.

When the case is an advanced one showing cardiac, pulmonary, or renal lesions, abrupt abstinence may entail general collapse, syncope of cardiac origin, and depressive psychic phenomena, melancholia, etc., of a very severe type. Here the dose of cocaine allowed should be only gradually reduced, and the patient meanwhile protected against the foregoing complications. The cardiovascular system especially should be watched and the normal *vis a tergo* of the blood-stream sustained with **caffeine** or **sparteine**. **Quinine** is also helpful and may be advantageously given with **iron** if, as is often the case, anemia is present. The stubborn insomnia which tends so severely to depress the nervous system should be met by the use of **trional** or other agents which do not depress the circulatory or respiratory system. A most efficient means against the tendency to collapse is a nutritious diet; this the patient soon learns thoroughly to appreciate, provided the meals are tempting and to his taste. Small quantities of easily digested food at short intervals are to be preferred. At the end of two weeks, the symptoms due to abstinence will have disappeared. Constructive metabolism should now be favored by means of **warm baths**, physical **exercise**, **massage**, and **actinotherapy**. André Lantheaume (*Revue de thé.ap.*; N. Y. Med. Jour., Jan. 25, 1913).

There is no need to "taper off" unless the patient is much debilitated, or has heart disease or severe kidney disease. The serious symptoms following sudden stoppage of the cocaine soon pass away, but there may be serious disturbances in the functioning of the bladder, heart and digestive organs, for a time, and the addict can scarcely ever hope to regain entirely his former physical and mental health. Children born after the father had become addicted to cocaine, may be idiotic or hydro-

cephalic. Vasoini (*Gaz. degli Osped. e delle Clin.*, Mar. 7, 1915).

After a study of about 12,000 cases the writers conclude that the treatment of such cases cannot be carried out except in a hospital or sanatorium. The gradual reduction method, so called, as practised by physicians outside of hospitals is condemned as useless. McGuire and Lichtenstein (*Med. Rec.*, July 29, 1916).

Though it is often asserted that three to six months suffice to effect a cure, but twelve months constitute the shortest time in which such a result can be hoped for. There are, at the same time, a few exceptional cases in which a good result has been secured in a shorter period.

As many cocainists will not apply for curative detention of their own accord, it ought to be the duty of the constitutional authorities to lay hold on these miserable and utterly helpless diseased persons, and insist on their reception and therapeutic seclusion for a given time, in a retreat, home, or hospital provided for the special treatment of such cases, with provision for persons with limited resources and for the very poorest. Such a provision would, in the long run, prove as economical as it would be invaluable to the welfare, physical and moral, of the whole community.

Cocaine has been employed to commit suicide. In the charters of various special institutions in the United States power is given to the managers to receive and compulsorily detain habitual inebriates who are addicted to excess in any narcotic or inebriant, including cocaine.

Cocainism has not come to an end since the enactment of the new law regulating the sale of cocaine, though somewhat more under control. This is because importation of the drug

by habitués themselves from other States and clandestine distribution are being carried on. It will continue until all the States take more practical and effective measures to overcome this abominable scourge. Biondi (Amer. Medicine, Sept., 1911).

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## COCAINE HYDROCHLORIDE. See COCA.

**COCAINOMANIA.** See COCA.

**COCCYGODYNIA.** See SPINE.  
DISEASES OF.

**COCCYX, DISORDERS OF.**  
See SPINE, DISEASES OF.

**CODEINE.** See OPIUM.

**CODLIVER OIL.**—Codliver oil is derived from the fresh livers of the cod, the *Gadus morrhua* of Linné, inferior qualities being obtained from other species of *Gadus*. According to the methods used for extraction, the oil varies from a pale yellow to a dark, brown-colored liquid. The pure oil is a thin liquid having a pale-yellow color, a peculiar fishy but not rancid odor, and a slightly acid taste. The specific gravity ranges from 0.918 to 0.922. The oil is slightly soluble in alcohol, but readily soluble in ether, chloroform, carbon disulphide, or 2.5 parts of acetic ether. The so-called alkaloids of codliver oil are absent in the fresh oils, but are found in the brown oils. They are decomposition products, ptomaines, or cadaveric alkaloids.

Codliver oil contains: *olein*, a fixed oil, about 70 per cent.; *palmitin*, about 25 per cent.; *gaduin*; *morrhual*, a crystalline substance having an uncertain composition; certain bile acids; small proportions of butyric and acetic acids; phosphorus and phosphoric acid; free fatty acids, as oleic, palmitic, stearic, and traces of iodine and bromine.

**PREPARATIONS AND DOSE.**—*Oleum morrhua*, U. S. P. (codliver oil), is given in the dose of 4 fluidrams (16 c.c.).

*Emulsum olei morrhua*, U. S. P. (emulsion of codliver oil), is composed of: acacia, 125 parts, and codliver oil, 500 parts, triturated with water, 250 parts, to which is added syrup, 100 parts; oil of gaultheria, 4 parts, and water, enough to make 1000 parts. Dose, 4 fluidrams (15 c.c.).

*Emulsum olei morrhua cum hypophosphitibus*, N. F. (emulsion of codliver oil with hypophosphites), contains: codliver oil, 500 parts; acacia, 125 parts; calcium hypophosphite, 10 parts; potassium hypophosphite, 5 parts; sodium hypophosphite, 5 parts; syrup, 100 parts; oil of gaultheria, 4 parts. Dose, 2 fluidrams (8 c.c.).

Owing to its disagreeable odor and taste, many patients object to taking this drug; it should therefore be given in as palatable a form as possible. Some patients prefer to take the oil in a small quantity of whisky, brandy, milk, or lime water; the addition of a small quantity of nitric acid sometimes makes it more palatable. The taste of the drug is oftentimes removed by eating a small piece of lemon or pickle just before and after taking it. Codliver oil may also be given in capsules, which are easily swallowed.

The digestion of the drug is increased when given in the form of a good emulsion, or by the addition of pancreatin, or when given in association with the hypophosphites. A good 50 per cent. emulsion is made by mixing 8 parts of the oil, 3 parts of condensed milk, 2 parts of glycerin, and a few drops of oil of bitter almonds; and equal parts of the oil and extract of malt rubbed together form a good emulsion for a child.

The two following formulæ serve to disguise the taste to a marked degree:—

Duquesnel's formulæ:—

*R Amber-colored codliver  
oil ..... 100 parts.  
Oil of eucalyptus ..... 1 part.*

M. This mixture tastes only of eucalyptus and is free from any disagreeable odor.

Brissemoret's formulæ:—

*R Codliver oil ..... ℥iiss (375 c.c.).  
Syrup of balsam of  
Tolu ..... ℥vj (180 c.c.).  
Tincture of balsam  
of Tolu ..... gtt. xij (0.75 c.c.).  
Oil of cloves ..... gtt. ij (0.12 c.c.).*

M. The mixture is not to be emulsionized, but simply shaken vigorously before the dose, a tablespoonful, is poured out. After it is taken, the only taste that remains in the mouth is that of the syrup.

Codliver oil is absorbed practically to the same extent when given either in the form of emulsion or pure codliver oil. Not only is the codliver oil absorbed, but it increases the absorption of other fats of the food to a marked degree. The use of codliver oil, especially in an emulsion, shows a remarkable saving of the proteid food in a comparative way. J. W. Wells (Brit. Med. Jour., Oct. 18, 1902).

**PHYSIOLOGICAL ACTION.**—Externally, codliver oil acts as a bland oil and emollient to the skin.

Internally, codliver oil increases the appetite, but has a tendency to cause disagreeable eructations, nausea, and sometimes diarrhea, especially when given in large doses. It is believed to be more rapidly absorbed from the intestines than other oils. It improves nutrition and its continued ingestion leads to an increase in weight and strength. It also increases the number of red blood-corpuscles and stimulates cell formation. The presence of phosphates makes the drug easily assimilable, and the association of the fatty bodies it contains with biliary matter promotes absorption and also aids in assimilation. Erythema or acne is sometimes produced by its use. Many of the alkaloids are said to stimulate the nervous system, and cause a rapid increase in the amount of urine and perspiration.

**THERAPEUTICS.**—**External.** — Rapid improvement is noticed when codliver oil is used by inunction in both children and adults suffering from wasting diseases, **athrepsia**, and in cases of defective nutrition, and its use may also be resorted to in children affected with chronic skin diseases, **marasmus**, and **tuberculosis**. It is said that inunctions to the chest give relief in **pertussis**, and are sometimes useful in **rheumatism** and **rheumatoid arthritis** when applied over the joints.

**Internal.**—The use of codliver oil internally is contraindicated in diarrhea,

hemoptysis, vomiting, aggravated dyspepsia, and high temperature. Providing these conditions are not present, it is of value in cases of **tuberculosis**, in acute diseases, especially in children, and in chronic diseases in which there is malnutrition and loss of flesh.

Codliver oil differs chemically from other oils and fats in that it is composed almost entirely of unsaturated fatty acids in the form of glycerides, together with traces of secondary products, possibly the result of putrefaction in the livers. From experimental evidence, it is extremely probable that one function of the liver is the preparation of fatty acids of a high degree of unsaturation for the further processes of metabolism; it might well be expected, therefore, that codliver oil would have some action on metabolism different from that of other fats. Williams has shown that it increases not only the total absorption of fat, but also the percentage absorption of all fats taken, and, further, that it influences the retention of nitrogen favorably. Codliver oil is clearly a different kind of food from other fats, such as cream and butter, and when general metabolism is abnormal it may supply a deficiency. Besides this action, it has been shown also that codliver oil *in vitro* dissolves the fatty envelope which surrounds the tubercle bacilli, and retards the growth of the organism.

While the oil is undoubtedly useful in the treatment of all wasting diseases, and especially phthisis, no evidence exists that it exerts any specific action on the tubercle bacillus in cases of well-developed and rapid tuberculosis. W. E. Dixon (Practitioner, Jan., 1913).

The writer ascribes the benefit from codliver oil to the fact that it supplies fat in an easily digestible and convenient form, while fat is the element of the food lacking most in the diet of the poor and of almost all children. When children already have a sufficiency of fat in the diet it

is folly to give codliver oil. This applies also to children with the exudative diathesis. The morbid tendencies of the latter are aggravated by fat in the diet; this was instructively shown in an experience at the children's clinic in his charge. He pushed codliver oil in treating a number of tuberculous children, giving them as much as they could take without appreciable disturbance. Some thus took up to 80 Gm. (2½ ounces) of codliver oil a day without apparent harm. The children did not make any special gain in weight on these large amounts of codliver oil, but one after the other they developed eczema of the face and scalp so that in a few weeks the clinic was a regular hotbed of "scrofula." The codliver oil was then dropped, and the tendency to eczema gradually subsided and has never been observed since at the clinic, as the writer's dietetic regulations keep the children permanently free from all such manifestations of the exudative diathesis, which is thus kept under control. Czerny (Therapie der Gegenwart, Feb., 1912).

It has been recommended, both internally and externally, in **rheumatism**, **gout**, and **rachitis** and wasting diseases of children. Certain skin diseases of strumous origin are benefited by it, and its employment in **strumous synovitis**, **caries**, and **necrosis of bone** is followed by good results. It has also proved beneficial in **tertiary syphilis**, **chronic bronchitis**, **emphysema**, and certain chronic diseases of the brain and nervous system. It may also prove of value in **epilepsy**, **chorea**, **neuralgia**, **paralysis agitans**, and **mercurial tremor**. It has likewise been found useful in combating degenerative changes and preventing failure in the nutrition of the brain in **atheroma** of the arteries.

The usual solution of phosphorus in codliver oil (1:10,000) is a specific in the **spasmophilia** of children. Five Gm. (20 c.c.) given twice daily for two to three weeks have caused disappearance of the attacks of **laryngismus stridulus** in 24 out of 32 cases, while only 2 out of 50 cases not

treated improved in this time. The writer experimented with a large clinical material to determine if the beneficial effect is due to the phosphorus or the codliver oil. Seven cases of **rachitis** were selected, and the improvement was measured by the diminution of the areas of cranio-tabes. The writer found that, while phosphorated codliver oil undoubtedly was a specific, phosphorus alone in oil or emulsion was ineffective. Codliver oil alone, on the other hand, when given in somewhat larger amounts (5 Gm.—20 c.c.—five times daily), had the same effect as a solution of phosphorus in codliver oil. He therefore recommends that such doses of codliver oil be given in all cases of rickets and spasmophilia. I. Rosenstern (Berl. klin. Woch., May 2, 1910). H.

### COFFEE AND CAFFEINE.—

The seeds or berries of *Coffea arabica*, so extensively employed for the preparation of the beverage, are not officially recognized except as the main source of caffeine.

### COFFEE.

This term, as is well known, is also given to the infusion of coffee used as a beverage. A fluidextract of the green berry was formerly employed as a stimulant, however, and the infusion is now considerably used for the same purpose in the treatment of shock, poisoning, etc. Hence its presence here as a remedy.

Before it is roasted, coffee contains *caffeine*, *cafeotannic acid*, and—according to Palladine—an additional alkaloid: *caffearine*. During the roasting process, however, a volatile oil is developed, which, with the other substances, termed collectively "*caffeone*," gives the coffee its agreeable aroma.

### PREPARATION AND DOSE.—

The infusion affects its users in dif-

ferent ways, some tolerating large quantities, others feeling the influence of one-half cupful. There is, therefore, no special dose to be recommended.

The fluidextract of green coffee (unofficial) may be given in doses of 1 to 2 drams (4 to 8 c.c.).

#### PHYSIOLOGICAL ACTION.—

The stimulating effects of coffee are due in considerable measure to the alkaloid *caffeine* (reviewed under the next general heading), of which it contains 1 to 1.3 per cent. Besides this active principle, however, coffee contains an empyreumatic oil, which also produces physiological effects.

According to Marshall and Hare, the percentage of empyreumatic oil obtained from an average browned coffee is 11.6 per cent.; in consequence, an ordinary breakfastcup of coffee contains about 45 minims (3 c.c.) of the oil, provided all the oil in the coffee used is extracted. In their opinion, the oil possesses none of the powers of a toxic character heretofore supposed. The pure oil increases the pulse rate by direct cardiac stimulation in small doses, and lowers pulse rate in large doses by a direct depressant effect on this viscus. On the highly developed spinal cord of the frog it causes increased reflex activity; but on the mammal with a well-developed brain, drowsiness and sleep.

The virtues of coffee, in the wear and tear of active life, are entirely subjective, and depend upon a general excitation of the higher centers, and chiefly upon its powerful exhilarant action upon the mental processes. It must be said, however, that the assumed ability of coffee to replace food, or to increase the power for work without corresponding tissue

destruction, is deceptive. While a moderate consumer of coffee may be assisted by the stimulating action of the beverage, an intemperate consumer may be capable of performing prodigious feats of strength and endurance, but, nevertheless, at the direct expense of his tissues.

The venders of coffee substitutes have, however, greatly exaggerated for obvious purposes the untoward effects of coffee, which occur only, as in everything, when it is used in excess by people who are oversensitive to its action, or where there exists a renal disorder. In epidemic febrile disorders in army practice patients do better when coffee is given them. It enhances resistance to the depressing influence of the disease. Notwithstanding the scare advertisements of health substitutes for coffee, there is no cause for apprehending danger to the race at large from coffee drinking. After generations of almost universal coffee drinkers, our own times see men of gigantic intellect in all realms of activity; our athletes are able to make sudden bursts of effort equal to any in history, and our soldiers acquit themselves manfully in fatiguing campaigns in torrid climes. The life-insurance companies, constantly warring against all that lessens longevity or conduces to abnormal organs, nerves, and actions, seem content to accept the use of coffee as one of the ordinary elements of everyday life.

Ingestion of coffee or fat-free cocoa is followed by an abrupt increase in the amount of gastric juice secreted. Tea has an opposite effect, tending to reduce the secretion. Pincussohn (Münch. med. Woch., No. 26, 1906).

Prosorowsky studied the influence of coffee and some of its substitutes

upon pathogenic micro-organisms, and concluded that coffee possessed incontestable antiseptic properties; in this respect it is superior to both its substitutes, rye and acorn coffee, the acorn being the more active of the two latter. The antiseptic action is due to the empyreumatic substances formed during roasting, and also partly to caffeotannic acids, the presence of which is alone capable of explaining the antiseptic action sometimes shown by infusions of raw ground coffee. A cup of coffee left in a room remains free from bacteria for over a week.

**POISONING BY COFFEE.**—The toxic effects of coffee, which are those of an excess of its empyreumatic oil and caffeine (*q.v.*), are illustrated by a case witnessed by Rugh, due to the drinking of large quantities of strong coffee. The patient's pulse was 96 and full, but weak; his respirations shallow and numbering 24 to the minute. The pupils were normal, the tongue slightly coated, the bowels regular; the skin moist, but not flushed; his expression was agitated with the fear of some impending danger. His muscles were in such a state of tension that, upon the slightest movement of arms or legs, clonic spasms occurred, though none was present when he lay perfectly relaxed, which, however, his exceedingly nervous condition would not allow him to do. If he tried to sleep, he would be seized with hallucinations just before losing consciousness, imagining that disasters were about to overtake him and seeing all kinds and shapes of images and objects. Then he would start up with fright and find himself in the greatest nervous excitement. When he stood up, he could close his eyes or look at the ceiling with-

out wavering. His knee-jerks were slightly exaggerated, but sensation was perfect.

Cohn witnessed a case in which two cupfuls of an infusion made of two handfuls of coffee produced intense general tremors, lasting, in spite of bromide treatment, twelve hours after all other symptoms had disappeared.

The writer observed the following cases:—

CASE I.—A large, heavily built, middle-aged man, who was in the habit of drinking one strong cup of coffee in the morning, another in the afternoon, and one in the evening, first noticed some dizziness which he could not account for. Also noticed that between meals he would feel weak and faint and have muscular twitchings, accompanied with intense hunger, to such an extent that he would be compelled to partake of some food or nourishment, when all symptoms would subside. No subsequent attacks after the use of coffee was discontinued and weak tea substituted.

CASE II.—A middle-aged man of the uric acid diathesis, which he tried to cure by exercise, baths, and saline laxatives, was quite elated over the fact that he had gone two years without a rheumatic attack and believed his treatment proper to ward off the attacks, which had been at yearly intervals, generally in the spring. In the fall of 1910 he noticed that around 11 o'clock in the morning, even though he had eaten a good breakfast, he would become suddenly seized with an uncontrollable hunger, accompanied by faintness, weakness, and tremblings, which would continue till he took into his stomach something in the line of nourishment, for example, milk, when he would promptly recover from the attack. Substituting weak tea for the coffee caused a subsidence of all these symptoms and he has been perfectly well ever since.

CASE III.—Mrs. S., aged 29 years, primipara; when she was about eight months pregnant, a friend asked her to have a cup of coffee. Although not a coffee drinker, Mrs. S. consented. In one hour's time she presented all the symptoms of coffee poisoning, as follows: face suffused and greatly swollen, welts all over skin of face and body, slight vomiting, extreme anorexia, sweatings, trembling of all the muscles, rapid heart action, anxious expression of countenance. Slow recovery from all these symptoms in four hours' time. Robert E. Coughlin (N. Y. Med. Jour., Aug. 5, 1911).

A case of severe chronic coffee poisoning, *i.e.*, coffeeism, was characterized by emaciation, premature wrinkles, a yellow complexion, tremor of the hands, lips, and tongue. The eyes are bright and quick; mydriasis is the rule; the demeanor is hesitating, brusque or uncertain, with involuntary movements, exaggeration of reflexes and neuralgias. This picture is very seldom complete, but nervous and digestive symptoms are comparatively common, and functional cardiovascular disturbance is still more frequent and important. The author has found the pulse small, hard and rapid, the arterial pressure high. The effects of chronic coffee poisoning may suggest gastric cancer, neurasthenia, or Basedow's disease. Roch (Arch. des Mal. du Cœur, Jan., 1916).

**THERAPEUTICS.**—Coffee infusion is a most valuable stimulant for cases of narcotic poisoning, as by **opium, acetanilide, hydrocyanic acid, aconite, antimony, corrosive sublimate, lead, mushrooms, tobacco, chloral hydrate**, and the later stages of **belladonna poisoning**. While it may prove effective when administered by the mouth, it acts with far greater rapidity when administered by rectal injection. It may be given *ad libitum* in such cases, and its effects will ap-

pear sooner in proportion as the infusion is strong.

The rapidity of absorption is enhanced if the temperature of the infusion approximates that of the intestine (100° F.—37.8° C.), since cold or heat produces momentary shock from which the intestinal walls must recover before the absorption can begin.

In the collapse of **anesthesia**, the toxic effects of **venomous stings and bites**, and **shock**, it is an invaluable adjuvant when employed by rectal injection. It sustains all the vital functions while the poison is exerting its effects, and carries the patient through the ordeal. According to Coughlin, dram (4 c.c.) doses of coffee without milk or sugar given every fifteen minutes are valuable in **vomiting after operations** and will be retained when everything else is rejected.

### CAFFEINE.

Caffeine is the active substance of the following plants: *Coffea arabica* (coffee) beans, in the proportion (as stated) of about 1 per cent.; *Thea sinensis* (tea) leaves, 1.5 to 4 per cent.; *Paullinia cupana* (guarana or Brazilian cocoa) seeds, 4 per cent.; *Cola acuminata* (kola nut) seeds or nuts, 2 per cent.; *Ilex paraguayensis* (maté or Paraguay tea) leaves, 1 per cent.

Caffeine should be obtained from the dried seeds of coffee, the coffee beans, but the caffeine of the drug-stores is really theine, since it is cheaper to manufacture the alkaloid from damaged tea than coffee. It is also closely allied to theobromine, found in cacao, coca, and other plants.

Caffeine is incompatible with potassium iodide, mercury salts, and tannic acid.

**PREPARATIONS AND DOSE.—**

The following preparations are official:—

*Caffeina* (caffeine; theine), occurring in small, silky needles, having no particular odor and bitter to the taste, soluble in 45.6 parts of water, in 53.2 parts of alcohol, in 375 parts of ether, and in 8 parts of chloroform. Dose, 1 to 8 grains (0.065 to 0.5 Gm.). A saturated aqueous solution of caffeine is neutral to litmus.

*Caffeina citrata* (citrated caffeine) is a fine white powder. It has a slightly bitter taste, acid reaction, is odorless, and soluble in about 25 parts of cold and 4 parts of hot water, and in a mixture of equal parts of alcohol and chloroform. It is made by dissolving 50 parts of citric acid in 100 parts of hot distilled water and adding 50 parts of caffeine. This is evaporated to dryness on a water bath and reduced to a fine powder. Dose, 2 to 12 grains (0.12 to 0.8 Gm.).

*Caffeina citrata effervescentes* (effervescent citrated caffeine) contains 40 parts of caffeine, 195 parts of citric acid, 570 parts of sodium bicarbonate, and 300 parts of tartaric acid. Dose, 60 grains (4 Gm.).

The following preparations, convenient for subcutaneous use because of their greater solubility than alkaloidal caffeine, are also recognized officially or semi-officially:—

*Caffeina sodiobenzoas*, U. S. P. (caffeine sodiobenzoate or sodium benzoate), a powder consisting of equal parts of caffeine and sodium benzoate, soluble in 2 parts of water. Dose, 2 to 15 grains (0.12 to 1 Gm.).

*Caffeina sodiosalicylas*, N. F. (caffeine sodiosalicylate or sodium salicylate), a mixture similar to the pre-

ceding, soluble in 2 parts of water. Dose, 2 to 15 grains (0.12 to 1 Gm.).

Another preparation, formerly semi-official, is:—

*Elixir caffeina*, N. F. III (elixir of caffeine), each dram (4 Gm.) of which contains 1 grain (0.065 Gm.) of caffeine. Dose, 1 fluidram (4 c.c.).

Caffeine, given by the mouth, does not, even in large doses, show its best effects. The hypodermic method is better, and is painless, producing no cutaneous reaction. The best preparation for this purpose is the caffeine and sodium benzoate above mentioned.

Hot, strong coffee is very efficient and presents the advantage of being readily available. It acts more rapidly when given per rectum than when used orally.

**PHYSIOLOGICAL ACTION.—**

Important in this connection is the fact that caffeine and related drugs are, chemically, derivatives of xanthin, which is one of the purin bases, similar to those which underlie the gouty diathesis, and which occur in the organism as a product of nitrogenous metabolism. Caffeine is a trimethylxanthin, while theobromine and theophylline, the other important members of the caffeine group, are both dimethylxanthins, but with the methyl groups at different positions in the xanthin molecule. Caffeine is but feebly basic, most of its salts being unstable.

**Nervous System.**—Caffeine stimulates the whole central nervous system, acting from above downward, *i.e.*, the brain and medulla first and then the spinal cord. Small doses act markedly on the intellectual centers, causing a more rapid flow of thought



and also disappearance of fatigue and drowsiness.

A series of experiments showed that caffeine produces a distinct increase in the capacity for muscular work, this increase being not due to the various physical factors which it was the special object of the research to exclude.

It became quite evident that a very considerable amount of variation is met with in different individuals; in some the rise in muscular capacity is not much greater than that which occasional variation might permit; in others, however, the increase in muscular capacity is very marked.

Variations of this character are found in conjunction with modifications as to time reactions. In one individual the heightened muscular capacity was more or less constant, while in another it set in very early, but was soon replaced by a decided fall toward the end of the experiment. W. H. Rivers and H. N. Webber (*Jour. of Physiol.*, Nov., 1907).

Careful psychological study conducted for forty days on 16 individuals, mostly students, whose ages ranged between 19 and 39 years. These were given, at different intervals, measured doses of caffeine mixed with sugar of milk and administered in capsules. In the subjects who were used as controls only sugar of milk was administered. None of the subjects knew at any time whether he was getting caffeine or not. In this manner the effects of expectation, suggestion, or enthusiasm in producing favorable or unfavorable results were eliminated from the experiments. In conducting the various tests the factors of fatigue, practice, time of the day, influence of meals, and the health and subjective sensations of the individual experimented upon were all taken into account. The results obtained were as follows: The typical motor caffeine effect was one of stimulation, sometimes preceded by a brief and slight initial retardation. The magnitude of the

stimulation, which began from forty-five to ninety minutes after the administration, varied directly with the size of the dose, up to 6 grains (0.4 Gm.), and was relatively slight when the caffeine was taken in the morning.

The steadiness test showed a slight nervousness following the administration of 1 to 4 grains (0.065 to 0.26 Gm.) of caffeine, and a pronounced unsteadiness following the administration of 6 grains (0.4 Gm.). This unsteadiness was greater if the caffeine was taken in the afternoon, and especially if unaccompanied by food. Small amounts of caffeine stimulated the power of co-ordination, while larger amounts caused a retardation of the latter. The speed of performance in typewriting was quickened by small doses of caffeine (1 to 3 grains—0.065 to 0.2 Gm.) and retarded by larger doses (4 to 6 grains—0.26 to 0.4 Gm.). The quality of the performance, as measured by the number of errors, was superior for the whole range of caffeine doses when compared to the quality yielded on the control days. In the color-naming test there was an indication of stimulation for the whole range of doses employed.

On sleep, doses of from 1 to 4 grains (0.065 to 0.26 Gm.) had no appreciable disturbing effects except in a few individual cases. Doses of 6 grains (0.4 Gm.) markedly impaired sleep, although a few individuals did not experience this effect, which was greatest when the drug was taken on an empty stomach and on successive days; it did not depend on the age, sex, or previous caffeine habits of the individual, but varied inversely with the increase in body weight.

As regards the effect of caffeine on the general health of the subject it was noted that irritability and headache followed the use of the larger doses. The two principal factors which seemed to modify the degree of caffeine influence were body weight and the presence of food in the stomach at the time of the administration.

The experiments showed the complete absence of any traces of secondary depression.

Caffeine may be contrasted with strychnine, which causes a secondary reaction of depression.

The toxicity of caffeine varies in different animals, and is less in the young than in the adult. The presence of pathological conditions increases the toxicity of the drug. H. L. Hollingworth (Columbia Contributions to Philosophy and Psychology, vol. xx, No. 4, 1912).

The effects of caffeine on the intestinal musculature appeared to be stimulation to the nerve centers which send impulses to the intestinal muscles, causing contractions that are not co-ordinated for peristalsis. There does not seem to be any increase in the activity of the reflexes in the intestinal wall causing the peristaltic wave which would push the mass of intestinal contents downward. The tendency is to intensify contractions which narrow the lumen of the intestine and add resistance to the passage of its contents. W. A. Frankland (N. Y. Med. Jour., Aug. 15, 1914).

Conversely, large doses cause restlessness, headache, vertigo, tinnitus aurium, and insomnia. Massive doses produce delirium, followed by stupor and other untoward effects described under Poisoning. On the spinal cord caffeine in large doses has an effect (seen especially in the lower animals) similar to that of strychnine; there is first increased reflex excitability, then tremors, then spinal convulsions, followed by paralysis if death has not already taken place from heart-failure. Caffeine has no peripheral nervous effect.

**Circulation.** — Caffeine stimulates the heart muscle directly, improving its tone and increasing its irritability. It also stimulates the vasomotor center and slightly so the vagus center.

The fall in blood-pressure brought about by small intravenous injections of caffeine is caused by a lowering of the tone of the vasomotor center by reflex action, without the aid of the depressor nerves. The blood-pressure-raising action of caffeine is in greatest part due to a *direct stimulation* of the vasomotor center in the medulla, and to a less degree of the centers in the spinal cord. Large doses of caffeine in dogs had no appreciable effect on the heart muscle. G. Swirski (Pflüger's Archiv, Aug. 22, 1904).

In dogs small therapeutic doses cause an increase of cardiac tone; the heart contracts more completely and its relaxation in diastole is less. There is vascular relaxation of peripheral origin, together with central stimulation of the vasomotor center, which usually leads to a rise in the blood-pressure. The end-result of this combined effect is a more rapid blood-flow and a greater mass movement of the blood. This suggests its clinical efficacy in cases in which the heart is dilated. It is to be noted that with larger doses the opposite effects are seen, the heart decreasing in tone and finally stopping in extreme distention.

The beneficial action of the drug would seem to depend upon the combination of factors which leads to a more rapid flow of a greater volume of blood through the organs and does not of necessity have an increased blood-pressure as a prerequisite factor. It was found that caffeine stimulates the heart directly and also stimulates the vagus center, thus tending to slow the otherwise faster rate. Both rate and depth of respiration are increased by therapeutic doses. Pilcher (Cleveland Med. Jour., Jan., 1912).

In a study of the effect of caffeine upon the blood-flow in 2 normal human subjects, both at rest and during work, the writers found that with increasing work a steady rise in blood-flow, oxygen absorption, and pulmonary ventilation occurred.

The increase in blood-flow was produced first by an increase in systolic output until a maximum of 118 c.c. was reached, beyond that by an increase in pulse-rate. During rest this action consisted in an increase in total blood-flow without a corresponding increase in oxygen absorption, and hence a decreased coefficient of utilization of the oxygen-carrying capacity of the blood. The pulse-rate was unchanged. Consequently the systolic output was increased. Means and Newburgh (*Jour. of Pharm. and Exper. Therap.*, Nov., 1915).

Moderate doses of caffeine tend, if anything, to slow the heart slightly and cause at the same time a slight rise of blood-pressure. Larger doses, on the other hand, tend to accelerate cardiac action and to increase the output of blood; this is a direct effect of caffeine upon the heart muscle, the restraining action of the vagus being now overcome. The blood-pressure then begins to be directly depressed by the drug. Still larger doses accelerate cardiac action to such a degree that diastole is greatly interfered with, causing the cardiac output to fall below normal. The final effect is auriculoventricular arrhythmia, the ventricles beating independently of the auricles, with weakening of the beat owing to beginning rigor of the heart muscle. Finally, paralysis of the heart occurs—the usual cause of death in animals poisoned with caffeine.

Caffeine causes cardiac stimulation or depression, according to the dose and rapidity of injection; increased heart rate, not due to vagus depression; vasodilatation, through peripheral depression of the vasoconstrictor mechanism; central vasoconstrictor stimulation is generally ineffectual. There occurs also convulsive stimulation and cardiac irregularities under

large doses. The early intravenous injections show the following phenomena: momentary myocardial depression, succeeded by myocardial stimulation; peripheral vasodilatation; central vasomotor stimulation, usually ineffective; increased heart rate. Blood-pressure: primary fall, followed by recovery and often a small rise. Oncometer: primary fall, followed by larger rise, usually outlasting that of the blood-pressure.

The summation of effects with cumulative doses of caffeine: (a) Total dosage of 20 to 150 mg. ( $\frac{1}{2}$  to  $2\frac{1}{2}$  grains) per kilo ( $2\frac{1}{4}$  pounds) shows: cardiac depression (dilatation); peripheral vasomotor paralysis; moderate and ineffective central vasomotor stimulation; heart rate reaches maximum and becomes irregular; blood-pressure falls to constant level of 50 to 70 mm.; fall of oncometer. (b) The blood-pressure reaches a constant level when the dosage reaches about 150 mg. ( $2\frac{1}{2}$  grains) per kilo ( $2\frac{1}{4}$  pounds) and further doses of caffeine may then be injected with little effect, but sudden cardiac failure may occur at any time. Sollmann and Pilcher (*Jour. of Pharmacol. and Exper. Therap.*, Sept., 1911).

**Muscular System.**—In keeping with its action on the circulation, which virtually means its action on the cardiovascular muscular elements, moderate doses of caffeine stimulate all muscles, increasing their irritability, the rapidity and power of the contractions, and their resistance to fatigue. Conversely, large amounts exert opposite effects and finally cause rigidity of the muscles, resembling rigor mortis, with complete loss of irritability. The beneficial effect of caffeine in those undergoing prolonged physical exertion is due both to its action on the muscles and on the nerve-centers.

**Respiration, Metabolism, and Temperature.**—Caffeine stimulates the

respiratory center, and thereby increases the intake of oxygen and the output of carbonic acid, this process being materially favored by the increased muscular activity induced, particularly that of the cardiovascular musculature. As a result nitrogenous metabolism is enhanced, sufficiently so when large doses are taken to cause a rise of temperature.

Caffeine in small medicinal doses, or in the form of 3 cups of coffee, affected diuresis but slightly, although the purin nitrogen was increased, while the amount and distribution of the nitrogen were not disturbed, thus showing that caffeine exerts no influence, in the doses given, on nitrogen metabolism in man. The caffeine did not apparently lessen tissue waste, and large doses would cause no marked effect upon nitrogen metabolism. Farr and Welker (*Amer. Jour. Med. Sci.*, March, 1912).

**Absorption and Elimination.**—Both these processes occur rapidly, caffeine being eliminated chiefly through the kidneys. When small doses are given, but little caffeine occurs in the urine unchanged; it loses its methyl groups in passing through the system at large, appearing in the urine as dimethylxanthin, monomethylxanthin, and urea.

Caffeine and theobromine act as direct excitants of the renal parenchyma. In contrast with the saline diuretics, which appear chiefly to provoke elimination of water and at the same time of salts, and especially chlorides, the xanthin bodies increase the elimination of nitrogenous elements, and especially urea and uric acid. Anten (*Arch. inter. de pharm. et de therap.*, vol. viii, fasc. v and vi, 1901).

Caffeine penetrates the organism rapidly, its effects are evanescent, and its elimination is rapid, chiefly by means of the bile and the urine.

The more the kidneys are diseased, the slower is its elimination. Zenetz found caffeine in the urine fifteen days after its administration had ceased. It acts upon the secreting cells of the kidneys, stimulating them and causing diuresis. Both the liquid and the solid constituents of the urine are increased by it, thus proving it to be one of our most efficient diuretics.

Caffeine is excreted in the urine to a very small extent as such. During its passage through the body it loses its methyl groups, and first becomes dimethyl, and then monomethylxanthin. Eventually xanthin is formed, and this breaks up probably into urea. In the urine are found small quantities of the unchanged drug, accompanied by larger quantities of dimethylxanthin, heteroxanthin, and xanthin. The most important property of caffeine from a therapeutic point of view is its power of increasing the secretion of urine. French (*Merck's Archives*, July, 1907).

Experiments upon nephrectomized rabbits showed that the amount of caffeine excreted was not diminished, the function of the kidney having been assumed by the gastrointestinal tract. It was also noted that there was no increase in the toxic effect of caffeine in the animals whose kidneys had been removed; in fact, it seemed that they were rather more resistant than the normal animal. The writer explained this on the ground that the removal of the kidneys caused the formation or the accumulation of substances which had a depressing effect upon the nerve-centers, thus rendering the animal less susceptible to the toxic action of the caffeine. Salant (*Trans. Amer. Med. Assoc.; N. Y. Med. Jour.*, June 15, 1912).

Caffeine is thought by some observers to be one of the drugs instinctively desired by man because of its exciting influences. In small, repeated doses, it may be advantageously prescribed to soldiers on the

march, as it increases muscular action and promotes the activity of the motor nervous system, both cerebral and medullary. The result of this double action is to diminish the sensation of effort and to prevent fatigue. It prevents shortness of breath, with resultant palpitation. In this manner it supplies vigor to one who is engaged in severe and prolonged exercise.

As far back as 1721 coffee was considered to "be excellent in the time of pestilence and contribute greatly to prevent the spread of infection." The writers review the work that has been done up to the present time in the study of the deodorant and antiseptic properties of coffee, and conclude their paper with an account of their own experiments in this field of research. Infusions of green coffee, they find, have no antibacterial properties. Infusions of roasted coffee have. The latter are able to inhibit putrefaction and prevent the growth of many bacteria, even in the most suitable culture media. To what coffee owes these qualities it is at present impossible to say. It is not probable that caffeine plays any part in the action of coffee upon bacteria. Crane and Friedländer (*Amer. Med.*, Sept. 5, 1903).

### POISONING BY CAFFEINE.—

Fatal caffeine poisoning is very rare. The main symptoms witnessed are marked excitement, enuresis, nausea, diarrhea with gastrointestinal pain, palpitations with rapid and irregular pulse, tremors, tetanic convulsions, collapse, and coma. Individual idiosyncrasy and various disorders increase the susceptibility to its action.

A diabetic suffering from a secondary grippal pneumonia received four hypodermic injections of a grain (0.065 Gm.) each in a day. As a result, there appeared agitation, loquacity, delirium, vomiting, cutaneous

and muscular hyperesthesia. Coma threatened, but there was no acetone or diacetic acid in the urine. The drug being omitted, all symptoms disappeared. M. Dalché (*Les nouveaux remèdes*, No. 7, p. 198, 1897).

James Ferguson observed a case of tonic spasm following a medicinal dose of citrated caffeine, repeated three hours later for severe headache, which became more violent than before. There was jerking of the hands and forearms, the fingers began to be rigidly clenched, and, shortly after, the head was seen to be drawn to one side, with the jaws tightly fixed together. At this stage the author found the fingers of both hands as described, and the muscles of the face tightly drawn, but with some imperfect articulation by this time possible. Friction of the affected parts did some good, and a dose of 30 grains (2 Gm.) of chloral hydrate was ultimately followed by recovery of control over the muscles. There had been no loss of consciousness throughout. The patient's sensation had been chiefly one of great faintness and nausea. The author suggests that the use of the drug be watched, since it has become a popular remedy for headache.

The toxicity of caffeine in the rabbit varies with the mode of its administration, being least when given by the mouth and greatest by intravenous administration. The toxicity is about from 15 to 20 per cent. greater by subcutaneous injection than by mouth, but is about half of this when injected into the peritoneal cavity.

The toxicity of caffeine is increased under some pathological conditions, since comparatively smaller doses proved to be fatal to rabbits, cats, and dogs, when marked lesions not due to caffeine were found at autopsy.

Glycosuria was observed in rabbits, guinea-pigs, and cats when caffeine was given in sufficient amounts. Salant and Reiger (Jour. of Pharmacol. and Exper. Therap., March, 1912).

**Coffeeism.**—While the habitual use of moderate quantities of coffee can have no deleterious influence in a normal adult, excessive quantities are prejudicial in the sense that morbid phenomena such as undue rapidity of the pulse, diuresis, and abnormal excitability are produced, all of which cease promptly, however, when the use of coffee is discontinued. Very large doses may produce, moreover, tremors, palpitations, pronounced digestive disturbances, and, occasionally, melancholia.

That the drinking of coffee may become a habit which causes a long line of symptoms may be seen by the following case reports. Guelliot, in 1889, reported his observations upon 23 cases of what he termed chronic *caféisme*, characterized by anorexia, insomnia, tremor of the lips and tongue, gastralgia, and various forms of neuralgia, dyspepsia, and leucorrhea. The features become thin and pinched, the skin pale or grayish yellow and wrinkled, the pulse weak, frequent, and compressible. Sleep is troubled by anxious dreams. Seventeen of the cases were in females. The evil effects of coffee were especially observable in children. Robert E. Coughlin (N. Y. Med. Jour., Aug. 5, 1911).

If caffeine is superadded to other toxic substances which tend likewise to produce excitement, alcohol, for example, the harmful effects of both agents—if these are taken immoderately—are enhanced.

Case of mixed alcohol and caffeine insanity. The patient, a man aged 52, was an intermittent drinker who had been sent to asylums twice for

alcoholic insanity; one of these commitments was voluntary. In the present instance he had taken 2½ quarts (liters) of Scotch whisky in four days, and, though not drunk, he realized that he must stop, and began to take caffeine as a bracer. He took 100 grains (6.5 Gm.) of the hydrobromide and citrate, with the result of producing a peculiar hallucinatory delirium, differing altogether from the ordinary alcoholic delirium in that there was a marked sense of well-being; the hallucinations were all of a pleasing character and he was more or less conscious of his condition. His appetite and general condition remained good. He soon recovered under treatment by isolation, liberal, non-stimulating diet, rather large doses of sodium bromide, with hypnotics at bedtime, and also suggestion, which seemed to be of value in this case. Large quantities of water were also given. E. S. Clouting (Jour. Amer. Med. Assoc., Feb. 22, 1908).

When small doses of caffeine and alcohol are combined, the result is generally a qualitative algebraic summation of both actions, i.e., that each drug produces, qualitatively, its ordinary effects. When large doses of the two drugs are combined, the effects of the stimulant drug tend to be reversed, the result being greater depression. In poisoning with fatal doses of alcohol, caffeine acts only deleteriously. With half-fatal doses, moderate doses of caffeine may decrease the narcosis and hasten recovery; large doses, however, are dangerous. In poisoning from "small" doses of caffeine, alcohol lessens the psychic effects; with large doses, alcohol adds to the danger. The danger of cardiac death is increased by agents which alone have relatively little depressant effect on the heart. This would engender caution in the use of caffeine in heart disease. Pilcher (Jour. of Pharmacol. and Exper. Therap., Jan., 1912).

Series of investigations to determine more exactly the effect of caf-

feine ingestion on the excretion of uric acid. Slight modifications of Benedict's method for determining uric acid make possible more accurate determinations than have hitherto been obtained. The addition of strong coffee infusion to a purin-free diet causes a marked increase in the excretion of uric acid.

The addition of a decaffeinated coffee product to a purin-free diet does not cause any increase in the excretion of uric acid. If, however, caffeine is added to a decaffeinated coffee, the excretion of uric acid is decidedly increased, as in the case of coffee. The increase in the amount of uric acid excreted under these conditions is equal to the quantity of uric acid which would be obtained by the demethylation and subsequent oxidation of from 10 to 15 per cent. of the ingested caffeine. Lafayette B. Mendel and Emma L. Wardell (Jour. Amer. Med. Assoc., June 16, 1917).

**THERAPEUTICS.**—Caffeine is of distinct advantage when the secretion of urine is deficient or to remove accumulated fluids or toxic substances. In **edema** due to heart disease its effect on the kidneys is valuable to supplement the indirect diuretic action of digitalis produced through the improved circulation. Coffee without cream or sugar is the more effective, but these additions are necessary in most cases to encourage its therapeutic use in such cases. Caffeine also stimulates the heart and tends thereby to counteract imperfect compensation in **valvular disorders**, but its action as such cannot be compared with that of digitalis.

In **ascites of hepatic origin** caffeine is also useful, though less so than in cardiac dropsy. In ascites of renal origin it is least reliable, the diseased renal tissue interfering with the action of the remedy. Nor is caffeine as useful as digitalis in renal disorders.

In **asthenic and degenerative heart disorders** and **adynamic functional disorders** of the same organ caffeine is often very beneficial as an aid to digitalis or to alternate with the latter if gastric untoward effects are awakened. Caffeine is further of great use in attacks of **dyspnea**, such as are observed in cases of **sclerosis of the coronary arteries**, and also in **cardiac insufficiency** following on **overexertion** and severe **mental shock**.

In clinical studies of the effects of caffeine in 15 patients suffering from advanced myocardial diseases, the writer found that in **myocardial insufficiency** with retained body fluid, caffeine causes a moderate increase in the urine output with a proportional loss of body weight. This increase reaches its maximum on the fourth day; a drop in both the systolic and diastolic blood-pressures which may stand in a causal relation to the diuretic coefficient, contrary to the usual teaching; a slight (3.6 per cent.) temporary rise in the pulse-rate, but no permanent change in either the pulse or respiratory rate; a moderate relief of the cardiac symptoms; the constant appearance of distressing nervous and gastric symptoms. The clinical diuretic action of caffeine may be better performed by large doses of theobromin sodium salicylate without the unpleasant side effects. L. Taylor (Arch. of Internal Med., Dec., 1914).

In emergencies caffeine is valuable as a stimulant to the medullary centers and to the cardiovascular musculature. Its action on the medulla is weaker than that of strychnine, but is more lasting, and even large doses show little or no tendency to cause secondary depression. It is of value in all forms of **collapse**, especially when the depression is marked, as in **poisoning by opium, alcohol, chloral hydrate, and toxic mushrooms**.

Caffeine is also useful where stimulation is necessary in **infectious diseases**, especially when the patient is in a condition of profound stupor due to toxemia, as may be the case in **typhoid fever, pneumonia, and diphtheria**. If there is mental excitement, however, its use is contraindicated. It is also indicated to counteract the **asthenia** which occurs late in febrile infections.

As a brain stimulant, caffeine is probably the least harmful agent available. In **neurasthenia, or asthenia** of nervous origin, it is often very efficient to counteract mental apathy and **psychasthenia**. The **apathy and stupor of infectious diseases** are also favorably influenced; this applies also to **depressive insanities**, such as **melancholia**, in which asthenia and deficient oxidation or metabolic activity prevail.

The power of caffeine to counteract drowsiness is utilized advantageously to oppose the dangerous somnolence caused by toxic doses of narcotic drugs, especially **opium**; it is of use in combating respiratory depression and preventing cardiac failure. Advanced **alcoholic intoxication** is also advantageously influenced.

Caffeine is efficient in the various forms of headache in which the pain is localized in a restricted area,—**migraine**, for instance. In general headaches due to cerebral congestion it is more harmful than beneficial. The efficiency of caffeine is enhanced when it is combined with one of the coal-tar analgesics: acetanilide, antipyrin, phenacetin (acetphenetidin), etc., or with the bromides. The official *pulvis acetanilidi comp.* (dose, 4 or 5 grains—0.26 or 0.3 Gm.) is often used, but the following is a safer com-

bination and one which is often more effective:—

℞ *Acetphenetidini* .... gr. xx (1.3 Gm.).  
*Caffeinæ citratæ*,  
*Camphoræ monobromatæ*,  
*Sodii bicarbonatis* .ää gr. x (0.65 Gm.).

M. et ft. capsulas no. x.

Sig.: Two every half-hour until relieved, not exceeding three doses.

Caffeine is valuable in **bronchial asthma** and in **bronchitis** associated with spasm of the bronchial tubes. When a paroxysm of asthma is present, Skerritt gives 5 grains (0.3 Gm.) of citrated caffeine every four hours until relief follows. When the attacks come on regularly in the early morning, a dose of 5 or 10 grains (0.3 or 0.65 Gm.) at bedtime often serves to avert them. No ill effects have followed the treatment, even when continued for years. The drug sometimes causes slight wakefulness, but, as a rule, patients go to sleep without difficulty after the nightly dose of 5 or 10 grains (0.3 or 0.65 Gm.).

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**COLCHICUM.**—*Colchicum corm* (*colchici cormus*), or meadow saffron, is the dried corm of *Colchicum autumnale* Linné, a perennial plant found wild throughout Europe. It contains not less than 0.35 per cent. of *colchicine*, an alkaloid, and the active principle: *veratrine*, starch, sugar, and gum. *Colchicum corm* usually occurs in transverse, reniform, or longitudinal ovate slices, the external surface being brownish in color and wrinkled in appearance, internally having a whitish color, transverse sections having a papillose appearance. It has a sweetish, bitter, somewhat acrid taste, slight odor, and is incompatible with all astringent preparations, tincture of guaiac, and tincture of iodine.



The **colchicum seed** (*colchici semen*) is the seed of *Colchicum autumnale*. It has a reddish-brown, finely pitted external surface, is whitish internally, and is very tough and hard. It has a slight odor and a somewhat acrid, bitter taste. With the addition of 6 to 8 per cent. of a fixed oil it has the same constituents as the corm.

Colchicine (*colchicina*) is the alkaloid and active principle of colchicum. It is a pale-yellow, amorphous powder, which becomes darker when exposed to light, and has a hay-like odor and a bitter taste. It is insoluble in petroleum benzin, slightly soluble in water, ether, or benzene, and readily soluble in alcohol or chloroform.

**PREPARATIONS AND DOSE.**—*Colchici cormus*, U. S. P. (colchicum corm). Dose, 4 grains (0.25 Gm.).

*Extractum colchici cormi*, U. S. P. (extract of colchicum corm), made by maceration and percolation with acetic acid and water, and evaporation. Dose, 1 grain (0.065 Gm.).

*Colchici semen*, U. S. P. (colchicum seed). Average dose, 3 grains (0.2 Gm.).

*Fluidextractum colchici seminis*, U. S. P. (fluidextract of colchicum seed), is made by maceration and percolation with alcohol and water, and then evaporation. Dose, 3 minims (0.2 c.c.).

*Tinctura colchici seminis*, U. S. P. (tincture of colchicum seed), made by maceration and percolation of 100 parts colchicum seed with 1000 parts of alcohol and water. Dose, 30 minims (2 c.c.).

*Vinum colchici seminis*, N. F. (wine of colchicum seed), made by maceration of 100 parts fluidextract of colchicum seed with 150 parts of alcohol and 1000 parts of white wine. Dose, 30 minims (2 c.c.).

*Colchicina*, U. S. P. (colchicine), is given in the dose of  $\frac{1}{228}$  grain (0.0005 Gm.).

Irritation of the fauces, a coated tongue, loss of appetite, flatulency, pain in the stomach, or diarrhea occurring while the drug is being given indicates that its use should be discontinued for a time, since these are toxic effects.

When a patient is taking colchicum the slightest gastrointestinal disturbance, especially diarrhea, is an imperative warning to discontinue the drug. All the remedies for gout on the market, the writer says, contain

more or less colchicum, and the gouty are liable to do themselves serious injury if they dose themselves without medical supervision. The writer has had 2 such cases of grave colchicum intoxication in his experience. It is our duty to warn gouty patients of this danger. Martinet (*Presse méd.*, Sept. 18, 1909).

**PHYSIOLOGICAL ACTION.**—When applied to the skin colchicum is an irritant, causing redness and smarting. Inhalation of the dust produces sneezing and conjunctival hyperemia and a burning sensation in the mouth and throat.

When given internally moderate doses usually have no appreciable effect upon the stomach and intestines, but sometimes their use is followed by nausea and diarrhea. If given over a long period of time colchicum impairs the appetite. Small doses are said to stimulate the secretory and excretory functions, and also act as a nerve sedative. Small doses of colchicine increase the amount of both urea and uric acid eliminated.

Colchicine, like muscarine, excites the nerve-endings in plain muscle, but has no action on those in the heart or in glands. Even in enormous doses, it is a slow poison, especially in herbivora; the delay is due to slow absorption into the central nervous tissues, and death is caused by vasomotor paralysis. It causes marked leucocytosis, the varieties of white corpuscles, which are increased, being different in carnivora and herbivora. There is increased activity of the bone-marrow, all the elements of which may be found in the circulation after large doses. Increase of leucocytosis, body temperature, and coagulation time of the blood run approximately parallel. W. E. Dixon and W. Malden (*Jour. Chem. Soc.*, June, 1908).

Experiments were made on the rabbit. The animal was weighed each morning before being fed. The urine was collected each day, and analyzed with a view to determine the output of urea, phosphoric acid, and chlorides. Colchicine was given in a

first series of experiments in doses of 0.001 to 0.0015 Gm. ( $\frac{1}{64}$  to  $\frac{1}{48}$  grain) per kilogram ( $2\frac{1}{4}$  pounds) of the animal's weight, hypodermically. Under the influence of the drug, the quantity of food absorbed by the animal was not modified. The caloric value increased from 200 to 201, and the urinary nitrogen, under the influence of colchicine, was increased from 0.295 to 0.410. The quantity of urine secreted rose from 32.9 to 49 Gm. ( $1\frac{1}{10}$  to  $1\frac{3}{8}$  ounces). The amount of phosphoric acid rose from 1.417 to 2.021 Gm. ( $21\frac{1}{2}$  to  $31\frac{1}{8}$  grains) and the chlorides from 0.1132 to 0.664 Gm. ( $1\frac{3}{4}$  to  $10\frac{1}{4}$  grains). The augmented catabolism thus shown explains the influence of colchicine in such affections as gout. Maurel and Arnaud (*Revue de pharmacol. méd.*, March, 1910).

**POISONING.**—Overdoses of colchicum produce vomiting, diarrhea, profuse perspiration, heat, and pain in the abdomen. The pulse becomes small, rapid, and thready. The respiration is slow, deep, and full at first, later becoming shallow, death occurring from respiratory failure. Consciousness usually remains unimpaired, but there is generally some vertigo.

Case of chronic poisoning by colchicine in a man aged 40 who had for a long while suffered from gout, and had been directed to take occasionally a granule of 1 mg. ( $\frac{1}{65}$  grain) of colchicine. Finding much relief, he had taken 4 or 5 of the granules per day. For some time he felt no special inconvenience, except 8 to 10 movements of the bowels daily. He developed the following symptoms, which were exhibited when the writer saw him. For thirty-six hours he had been almost unable to move and was nearly voiceless. The skin was cool and the temperature below normal. There was thirst and nausea. The pulse was small and thready. The urine was much reduced in amount, but free from sugar or albumin. The bowel movements were 30 to 40 in the day and profuse, containing white, flocculent matter. A

tendency to vomiting was also exhibited. Frequent spasmodic movements of the general muscular system occurred, and touch excited violent and painful contractions. The pupils were not affected and the speech was not disordered. The patellar reflexes were increased. It was evident that a condition of chronic poisoning by colchicine had been developed. The use of the drug was stopped, injections of normal salt solution and sparteine sulphate were employed, and a milk diet advised. The condition noted above lasted for twenty-four hours, when an abundant secretion of urine was established; the muscular symptoms abated steadily and passed away in about fifty hours; the profuse diarrhea also ceased. It seemed that the patient was out of danger, but on the fifth day the physician was suddenly recalled, to find the man suffering from fever (temperature  $103^{\circ}$  F.— $39.4^{\circ}$  C.) and swelling of the joints, with severe pain. The urine was of moderate quantity, but there was no bowel movement. Various salicylates were administered and a strict milk diet ordered. The normal condition was restored in several weeks. Mabilie (*Bull. gén. de thérap.*, No. 8, 1902).

Severe case of poisoning by 2 "Blair's gout pills," which, as is well known, contain extract of colchicum. The patient had a typical abdominal facies; lips and nails, bluish; respiration, quick and shallow; pulse, small and quick; skin, pale and clammy. He vomited a large amount of yellow fluid and had several profuse and bloody passages from the bowels. The temperature was  $96.5^{\circ}$  F. ( $35.8^{\circ}$  C.). Under sedatives and carminatives the patient recovered. A month before, the same patient had taken 2 of the same kind of pills with similar, but much less intense, symptoms. L. G. Davies (*Brit. Med. Jour.*, Nov. 14, 1903).

**Treatment of Poisoning.**—The patient should be kept in the recumbent position, and the stomach emptied by means of

emetics and the stomach pump. Demulcent drinks and large doses of tannic acid are very helpful. It may be necessary to give morphine to relieve the pain, and, should collapse occur, external heat and stimulants are indicated.

**THERAPEUTICS.**—Colchicum is used extensively in the treatment of gout, its administration being decidedly beneficial in the greater number of cases. Colchicine is believed to be more successful than any of the forms of the crude drug. Full doses of the drug should be given during the attack, although frequently causing nausea and vomiting, and smaller doses between attacks. Large doses during the attack give almost immediate relief, while small doses are not effectual for several days.

Colchicum is also found useful in rheumatism, bronchitis, asthma, and the cutaneous disorders occurring in gouty subjects.

During an attack of acute gout colchicum is of great value, as digitalis is in certain affections of the heart. It is this action of colchicum which has made it a specific medication in gout. In the interval between attacks, when the premonitory signs of an attack appear, colchicum should be given to abort the attack. In chronic gout colchicum is not of such great service. Martinet (*Presse méd.*, July 31, 1909).

In periods other than acute gout, when the elimination of uric acid is less abundant, colchicine ought also to be prescribed from the very beginning of the attack, for, while in the longer or shorter intercalary period between an acute attack of gout and the chronic phase of it, which may be called subacute, the quantity of the uric acid excreted reaches at times from 80. to 90 cg. per liter at the maximum, it never exceeds from 55 to 60 cg. (9½ to 10 grains) per liter (quart) in chronic gout.

It is therefore not alone the elimination of the uric acid which is to be considered by the physician during a period when the gouty diathesis has made further progress, but he

must think of the evil action which this diathesis may yet have upon the viscera. For it must not be forgotten that the gouty person dies of trouble with his heart or his kidneys, and it is this final fatal term which should be retarded as long as possible, by preserving the organs against the more or less violent assaults of gout, repeated or prolonged. Constant (*Jour. de méd. de Paris*, Sept. 25, 1909).

In chronic rheumatism and rheumatoid arthritis it is advisable to give the drug in conjunction with potassium iodide. Colchicum should be given with caution in elderly persons and those having a feeble circulatory system. C. Abadie has used ¼ grain (0.001 Gm.) of colchicum in scleritis with good results, and F. Woodbury recommends its use hypodermically in muscular rheumatism and sciatica. It is sometimes of value in gonorrhea. H.

**COLD.**—As a remedial agent cold is nearly always available and is of great value in many disorders.

**PHYSIOLOGICAL ACTION.**—When first applied, cold produces some congestion of the superficial blood-vessels, rapidly followed by their extreme contraction and a lowering of the surface temperature. Pain is relieved by its application, because the cold depletes the painful area of its arterial blood, and in this way relieves the pressure on the nerve-endings. Prolonged application of cold compresses completely arrests sensation, so that cold is sometimes used for anesthetic purposes. Cold is also used to control inflammation and sometimes as a hemostatic.

A cold bath first causes, in a healthy individual, shivering and a feeling of extreme cold. The extremities become blue and covered with *cutis anserina*, and the abstraction of heat lowers the bodily temperature. Reaction immediately follows: there is a redilatation of the capillaries, the extremities grow warm, the body surface becomes flushed, the frequency and force of the pulse is increased, and the respirations become full and regular. A general feeling of exhilaration is experienced, which lasts for many hours. Should the in-

dividual remain in the water too long, he again feels cold, and the nervous and circulatory systems become depressed. Weak and debilitated individuals react very slowly to the application of cold, reaction sometimes being entirely absent.

By inserting a narrow thermometer in the lower end of a stomach-tube, the end only projecting, the writer was able to determine the temperature in the interior of the stomach before and after application of cold outside. He found that the temperature could be thus reduced by  $1.8^{\circ}$  C. ( $35.2^{\circ}$  F.) in the stomach and  $1.1^{\circ}$  C. ( $34^{\circ}$  F.) in the rectum. This reduction of nearly  $2^{\circ}$  C. ( $35.6^{\circ}$  F.) in the interior of the body may prove of life-saving value. Riehl (Münch. med. Woch., Dec. 27, 1910).

The effect of cold air on the body is twofold. First, there is an actual extraction of heat which is rarely desirable, and as far as possible should be prevented. The body loses the largest amount of heat through conduction and this should be prevented by proper clothing. Much more important than the abstraction of heat from the body is the stimulating action of the cold on the delicate sentient nerves of the periphery. Both respiration and circulation are strengthened, oxidation is increased, and nutrition becomes more active. There is also a powerful stimulation conveyed to the medullary centers by the effect of cold air on the nasal mucous membrane. Cold, provided it be not excessive, has a markedly stimulating action on the digestive system. Cold also seems to stimulate the blood-forming organs. As a result of these factors, the resisting powers of the body against toxins and its ability to respond protectively to the assault of infection are greatly increased. These benefits of cold depend, however, on the power of the individual to react, and this varies greatly and seems to be dependent on the vasomotor tone. Those suffering from any interference with the free passage of air through the nostrils do not react well to cold

air. Inflammatory conditions of the larynx and trachea may be subjected to additional irritation by cold air. To benefit from a winter in the North, the intestinal tract and the kidneys should be in good working order. Extreme cold is not desirable for those suffering from gout, arthritis, or neuritis. For those suffering from advanced degeneration of any organ, for those advanced in years, and for the very young extreme cold may be distinctly harmful. A. S. Blackader (Amer. Jour. Med. Sci., Aug. 10, 1912).

Contrary to the generally accepted belief that cold inhibits the proliferation of germs but does not destroy them, the writer's experiments showed that sufficiently long exposure to cold will destroy the cultures beyond possibility of recuperation. The temperature was dry cold and kept constantly between  $-3^{\circ}$  C. and  $-12^{\circ}$  C. Thirty cultures of colon bacilli and other germs were placed in the refrigerator and some were withdrawn on successive days and incubated. By the fourth day only from 3 to 49 colonies developed, instead of the thousands of the second day, and no colonies at all developed after the fourth day. A. Q. Ruata ((Annali d'Igiene, Jan., 1918).

**UNTOWARD EFFECTS.**—Prolonged exposure to cold produces local or general devitalization. Complete restoration of function never follows complete freezing; the part, becoming necrotic, sloughs off, causing *gangrene* (*q.v.*). Less intense cold tends to cause permanent dilatation of the capillaries of the skin, with paresthesia and sometimes itching, causing *chilblain*, or *pernio* (*q.v.*). Prolonged exposure to cold causes shriveling and lividity of the skin, muscular weakness, and rigidity. At first there is drowsiness and confusion, later coma. The pulse and respirations become slow, the pupils dilated, and death finally occurs, probably due to cerebral anemia from failure of the circulation.

Cold inhibits the growth of bacteria and kills some, but even immersion in a freez-

ing solution does not kill all pathogenic organisms. Spores usually resist the action of cold.

**Effects of cold on infected animals.**

Animals in the cold chamber were livelier than those in the animal house, and the fact that the majority of these gained weight shows a favorable influence on nutrition. Experiments in rats and guinea-pigs inoculated with *T. gambiense* and *T. rhodesiense* show: (a) Delayed incubation in the cold. (b) Prolongation of life in the cold. (c) Tendency for fewer parasites to occur in the peripheral blood of animals kept in the cold. Incubation period of *T. lewisi* and *T. brucei* was delayed in the cold. There was prolongation of life of animals infected with *cadaras* and *nagana*. It was noted in 2 guinea-pigs after inoculation with tubercle that the superficial abscess which formed at the site of inoculation developed much more slowly in the cold (a month later). In rats infected with *Spirochata duttoni* the numbers of parasites circulating in the peripheral blood were fewer in the animals treated in the cold chamber, and this was also observed in guinea-pigs infected with *T. brucei*. Thompson and Ross (Brit. Med. Jour., March 25, 1911).

**THERAPEUTICS.**—Cold compresses are used in nearly all congestive disorders, as in severe congestive headaches. Cold compresses or the ice-bag is used in pneumonia, controlling the inflammatory process and relieving pain, but, where the temperature is quite high in this disease, a cold bath is sometimes given. Cold compresses are of much value in tonsillitis, pharyngitis, and laryngitis, and small pieces of ice allowed to melt in the mouth do good in the various inflammations occurring in that cavity. Cold compresses give almost immediate relief in sprains if pain is present and they do much to limit the inflammation in certain acute eye diseases.

The ice-bag is useful in acute pericarditis. Lees, of London, says that it tends to check the violence of the inflammation, re-

strict the effusion, and is usually liked by the patient. It is also of value in acute inflammations of joints and to relieve the severe pain of appendicitis.

The cold douche is of great value in exciting respiration in the newborn. Cold water poured upon the abdomen will sometimes excite contractions of the uterus in cases of uterine inertia, and cold along the spine may be tried in suppression of urine. Attacks of hysteria are often relieved by the application of cold either locally or generally.

The so-called "drip-sheet" has a most marked tonic effect in certain neurasthenic cases. A sheet, dipped in cold water, is thrown around the patient and brisk friction is then applied to the entire body.

Freezing, especially by liquid air, has been used to stimulate granulations in varicose ulcers, chancroids, specific ulcers, lupus, and many other conditions.

First case of cancer in which the writer used freezing. The neoplasm was a myosarcoma in the adductors of the thigh. He inserted the tip of a dressing forceps into the center of the tumor, after cocaine, down to sound tissues, and then opened the blades of the forceps and sprayed with ethyl chloride in the cavity thus formed. The pressure of the forceps expels the blood from the parts and facilitates the freezing. The procedure was repeated at various points in the tumor and the deep freezing was repeated every third day for six times in all. Suppuration and healthy granulations followed and the tumor gradually healed. Superficial freezings were continued every third day and the patient was dismissed, clinically cured, forty-nine days after commencement of the treatment. He returned in January with metastases, both local and elsewhere, to which he succumbed in May. C. A. Dethlefsen (Hospitalstidende, June 18 to July 9, 1902).

The continuous application of cold is a valuable adjunct to the treatment of malignant tumors. The pains will lessen, the tumor will diminish in size, and the discharge will often

lose its disagreeable odor. After-effects, such as diarrhea or neuralgia, will rarely be complained of. Superficial carcinomata are preferably covered with ice-bags; in carcinoma of the stomach and mouth pieces of ice are swallowed, while in neoplasms of the abdominal organs coils are placed upon the abdomen. The effects of warmth are just the opposite. Keating-Hart (Journal de prat., No. 16, 1908).

White used liquid air for the stimulation of **ulcers**, and for producing **anesthesia** for surgical purposes. For the latter purpose it acts quicker than ethyl chloride. It is sufficient to produce only a superficial freezing. Some have used this anesthetic action to quiet the pain of **zoster**. Here the cold is applied to the spine. He advocated its use for the treatment of **boils** and **carbuncles**, and applied liquid air for this purpose in the form of a spray from a bottle with a cork perforated to let 2 glass tubes pass through. When the finger was placed over the shorter tube, the air came in a fine stream of spray from the other tube that went down into the liquid. In this way the air was forced into the openings of the carbuncle or boil, and the surface was slightly frozen. Many of Dr. White's early experiments were made at the Vanderbilt Clinic.

The best treatment for **lupus erythematosus** is freezing. Every case of this most intractable disease has been cured when the patient has submitted to complete treatment. The disease is capricious, and recent cases often yield to other remedies and disappear without a scar. It is best then to try other simpler remedies in recent cases. But in chronic patches, where there has been more or less deep destruction of tissue, freezing is the remedy of choice. Of course, it does scar, but the scar is soft and pliable, and the disease is sure to scar of itself. The writers have seen patches heal after a single freezing. In this disease it is not necessary to freeze deeply. When the cone is dipped

in ether, fifteen seconds is usually enough. **Pigmentary nevi** are easily removed. **Hairy nevi** also must be frozen deeply, using firm pressure for one or two minutes, so as to destroy the hair-follicles. Though they may have to be frozen several times, at last the result is a brilliant one. **Epitheliomata**, especially of the **rodent-ulcer** type, are more rapidly cured by freezing than by any other form of caustic, and with less pain, and the scar is of the best. In them the pressure must be firm, and the time of freezing from half a minute to a minute and a half, depending upon the depth of the ulcer and the thickness of its walls. Other forms of the disease may be cured by it, and in inoperable cases it should always be tried. **Keratosis senilis** is readily removed by freezing. **Warts**, **papillomata**, **tattoo marks**, **powder stains**, **hypertrophied scars**, **keloid**, **tuberculosis verrucosa cutis**, **chloasma**, and **scrofuloderma** have all yielded to freezing. The authors believe that Dr. White's application of freezing with liquid air as a therapeutic agent is one of the most important of our time. Jackson and Hubbard (Med. Record, April 17, 1909).

The *cold bath* is employed in the treatment of febrile conditions, particularly **typhoid fever** (*q.v.*). It is used in this disease for the marked diuresis it produces, to reduce temperature and stimulate the nervous system. During a cold bath, brisk rubbing of the entire body should be carried out, and the feet should be kept warm. Cold baths are sometimes of value in **enterocolitis**, and in **acute rheumatism** with high fever. The temperature of the bath should be made at first about 85° F. (29.5° C.), and the temperature lowered 5° F. (2.8° C.) at each successive bath until 65° F. (18.3° C.) is reached. Cold douches, affusions, baths, and the drip-sheet, systematically used, are of much value in the treatment of **tuberculosis**.

The use of cold is contraindicated in weak or very old persons, and in fevers if the pulse is weak and feeble, the skin cool and clammy, and when delirium is present.

H.

**COLD BATHING.** See WATER (HYDROTHERAPY.)

**COLEY'S FLUID.**—Fehleisen, Coley, and others noticed that erysipelas occurring in persons having malignant disease was followed by improvement and sometimes disappearance of the tumor. This suggested inoculation with the streptococcus of erysipelas in the treatment of such tumors.

Coley first used injections into the tumor of living cultures of *Streptococcus erysipelatis* grown in bouillon. This was followed by improvement, especially in sarcoma. Following this, in 1872, he used the toxins instead of the living culture. The bouillon cultures were sterilized by heat at 100° C., and then injections given directly in the tumor. Then he experimented by using for injection the filtrate produced by passing the living culture through a Kitasato filter. In this case the reaction was much less severe and the growth of the tumor inhibited. Wishing to increase the virulence, Coley combined the *Streptococcus erysipelatis* and the *Bacillus prodigiosus*.

The writer's treatment of sarcoma with the mixed toxins of erysipelas and *Bacillus prodigiosus* which he instituted sixteen years ago is based upon the following accepted clinical facts: (1) That inoperable sarcomas, and even carcinomas, have been known to disappear and the patients to remain well and permanently cured as the result of accidental erysipelas. (2) That inoperable sarcomas have disappeared as a result of attacks of erysipelas produced by inoculation. In all, the writer himself has treated about 430 cases of sarcoma with the mixed toxins. In 47 of these cases the tumor has completely disappeared, and in 28 cases a period of from three to fifteen years has passed since the disappearance; 26 patients have remained well from five to fifteen years. These figures cover a period of fifteen years, and during this period important improvements have been made, from experience, in both the preparation of the toxins and the method of ad-

ministration. There is no appreciable risk from this treatment. In only 3 out of the 430 cases death could possibly be attributed to the toxins. These 3 patients were in the last stages of the disease, with extensive metastases and very feeble heart action; 2 of the cases presented extensive involvement of the mediastinal glands, and in both the treatment had only just been begun, for two or three days, and sufficient doses had not been given to produce any marked reaction. The patients died suddenly, apparently as a result of an embolus. Coley (Boston Med. and Surg. Jour., Feb. 6, 1908).

**PREPARATION AND DOSE.**—In preparing Coley's fluid as it is now used, a virulent culture of the streptococcus of erysipelas is obtained, preferably from a fatal case of erysipelas. This is inoculated into slightly acid bouillon, and allowed to grow for about three weeks. The bouillon is then reinoculated with the *Bacillus prodigiosus*, and allowed to grow another ten days. The flask containing the bouillon cultures is then well shaken, the bouillon poured into half-ounce bottles, and sterilized by exposure to heat of 50° to 60° C. for one hour. It is then used without filtering except in children and the debilitated, in which filtered toxins are used.

**Dose.**—The dose of the fluid should be small at first, 1 minim of the filtered or ½ minim of the unfiltered toxins being used. Each day the dose should be increased ¼ minim until the reaction temperature is 103° to 104°. The frequency of the injections depends upon the general condition of the patient.

If no result is observed after using the fluid for three weeks it should be discontinued. The injections may be continued for several months in successful cases, allowing a few days' rest at various intervals.

**PHYSIOLOGICAL ACTION.**—Following the injection of Coley's fluid there is a decided reaction. There may be a chill fifteen minutes to one hour after the injection, which may last from fifteen to forty-five minutes. Nausea, vomiting, and

headache usually occur, and the temperature may reach 103° to 104°.

If the treatment is successful there is usually noticeable improvement within a week. There is a marked decrease in the vascularity of the tumor; there is a loss of the smooth, glossy appearance of the overlying skin, which becomes wrinkled. The tumor becomes more mobile and loosely attached.

Case in a woman 45 years of age who had a fusiform swelling of regular outline and well-defined limits in connection with the lower part of the right humerus, with no suspicion of fluctuation or egg-shell crackling about it; the skin and muscles were not implicated, but the superficial veins were a little prominent and there was an enlarged gland in the right axilla. The arm was wasted and the muscles were weaker than those of the opposite side; the movements of the elbow-joint were unimpaired. Pain was only complained of when using the arm or on applying firm pressure. No other bone abnormality could be made out. There was no history of injury or of fracture, and the question of syphilis was carefully gone into, but no evidence of it could be obtained. Treatment with Coley's fluid was given. He began with ½-minim (0.03 c.c.) doses and increased them by ¼, ½, and 1 minim (0.015, 0.03, and 0.06 c.c.) until a maximum of 9 minims (0.54 c.c.) was reached; the first injections were given into the arm outside the limits of the growth, but the later ones were injected into it, and 23 injections in all were given. They were followed by pain and swelling at seat of injection, with general malaise, headache, nausea, vomiting, and pains in the limbs and joints, followed by the appearance of subcutaneous hemorrhages resembling bruises, but with only slight rise of temperature and increase of pulse rate. These after-effects were very unpleasant. The swelling disappeared and the structure and outline of the bone resumed its normal appearance. Ashdowne (Lancet, May 22, 1909).

**THERAPEUTICS.**—Coley's fluid has been used in carcinoma and sarcoma, but with practically no success in the former. It is used in the inoperable cases of sarcoma, the most marked results being seen in the spindle-celled variety. Its action is less effective in the mixed-cell and osteosarcoma, and is of least value in the melanotic form. If there is no return of the tumor within three years, the patient is usually cured. See also the article on CANCER in the second volume.

The writer has had cases of inoperable sarcoma in which the tumors disappeared under the use of mixed toxins of erysipelas and *Bacillus prodigiosus*. The utmost efforts have been made to trace the after-histories of these cases, with the following results: 7 remained alive and well at the end of fifteen to eighteen years; 7 remained alive and well at the end of ten to fifteen years; 17 remained alive and well at the end of five to ten years; 10 remained alive and well at the end of three to five years. That is, 41 cases remained well from three to eighteen years, or 31 from five to seventeen years. As to the correctness of the diagnosis in these cases, they were, to all intents and purposes, selected cases, i.e., selected by the leading surgeons of America, as hopeless, inoperable cases. In all of these cases, with exception of 4, the diagnosis was confirmed by careful microscopic examination, in most cases not by one, but by several of the most competent pathologists. In order still further to eliminate all chance of error in diagnosis in a large number of the cases, there was a history of very rapid growth and repeated recurrence after operation. The writer also noted a small number of cases in which, after the complete disappearance of the tumor under the toxin treatment, the disease afterward recurred locally and generally and caused the death of the patient. Coley (Surg., Gynec., and Obstet., Aug., 1911). H.

**COLITIS.** See **INTESTINES, DISEASES OF.**



**COLLARGOL** (*collargolum, argentum Credé, or argentum colloidal*) is metallic silver in colloid form. It was originally recommended by Credé, of Dresden. It is said to contain 85 to 87 per cent. of silver and a small percentage of albumin, with the products of oxidation. It occurs as small, brittle, hard pieces, scale-like in appearance, and having a bluish-black color. It forms, with 20 parts of water, a dark, olive-brown, colloidal suspension, which remains stable for some months. Precipitation by acids and salts is prevented or delayed by the addition of albumin to collargol; therefore, during its manufacture, a sufficient amount of albumin is added to prevent its precipitation under ordinary circumstances. A collargol suspension should not be exposed to light or air. It is incompatible with the usual silver reagents. The drug is not official.

**PREPARATIONS AND DOSE.**—For local use, collargol is used in the form of the *unguentum Credé* (colloidal ointment), which contains about 15 per cent. of collargol. It consists of 15 parts of collargol, 5 parts of water, 10 parts of white wax, and 70 parts of benzoinated lard. This ointment has naturally a dark, bluish-gray color, turning to a brownish hue upon the addition of water. The ointment is good as long as it stains the skin black. A 1 per cent. colloidal suspension may be used as a wash, and it may also be used as a 5 per cent. dusting powder.

Internally, 1-fluidram (4 c.c.) doses of a 1:500 to 1:100 solution (colloidal suspension) may be given. A 2 to 5 per cent. suspension may be used for intravenous injection, a method preferred by many at the present time.

**PHYSIOLOGICAL ACTION.**—Collargol is said to be a systemic antiseptic and germicide, and to have a similar action to silver nitrate, but practically devoid of the irritant and corrosive action of the latter drug. The beneficial effects have been mainly credited to the production of leucocytosis, which enhances phagocytosis.

The intravenous injection of collargol caused an increase of leucocytes in 6 experiments and more bacteria than normal were taken up by them; but the opsonic index was not

influenced. Hoffmann (Berl. klin. Woch., Feb. 15, 1909).

**THERAPEUTICS.**—In **septicemia** the collargol ointment may be used by inunction, 30 to 60 grains (2 to 4 Gm.) being thoroughly rubbed into the skin at each time. The suspension may be used for irrigating the bladder in **chronic cystitis**, and for **surgical dressings**, the strength depending upon the condition present.

Colloidal silver within the past few years has been administered hypodermically, by the stomach, and by inunction in the treatment of various forms of localized and general **septicemia**. The writer is firmly convinced of its efficacy. In the acute enlargements of the lymphatic tissues of the neck which may follow scarlatinal, diphtheritic, and other forms of **tonsillitis**, collargol ointment, properly rubbed into the surrounding lymphatic tissues, is of value in preventing the spread of the disease and in controlling the localized sepsis. This drug can be given more efficaciously to infants and young children by inunction than in any other manner, and its value in combating general and localized **sepsis** is greater in infants and children than it is in adults. B. K. Rachford (Amer. Jour. Med. Sci., Jan., 1909).

Internally, collargol is said to be of value in **gastric ulcer** and other gastrointestinal diseases in which silver nitrate is used.

In cases of **acute erysipelas**  $\frac{1}{3}$  grain (0.02 Gm.) two or three times a day may prove of value.

Credé's ointment of collargol limits inflammation and cuts short suppuration in such diseases as **dacryocystitis**, **abscess of the lid**, **boils**, or **styes**. In **blepharitis** it has a real advantage over the ordinary yellow ointment, especially when the patient has an idiosyncrasy to mercury. Simple **conjunctivitis**, both acute and chronic, showed a tendency toward rapid healing; in membranous conjunctivitis the membrane separated with unusual rapidity, and the cornea recovered without any lesion. Its

power of exciting resorption was shown by its effects on old scars. Feilchenfeld (Woch. f. Therap. u. Hyg. des Auges, Oct. 13, 1904).

The diseases in the treatment of which collargol has found employment are divided by the authors into two groups—those in which their own experience and that of others fully convinced them of its therapeutic efficiency, and those in which they consider its action doubtful, although successes have been reported.

Signal success was obtained in **purulent pleurisy** and **septicopyemia** following **typhoid fever**, in **pyelonephritis**, urinary and genitourinary affections, **phlegmons** and local inflammations, malignant **syphilides**, **tuberculous foci**, **puerperal septicemia**, **septic endocarditis**, **paratyphoid fever**, and **tuberculous enteritis**.

The action of collargol is considered doubtful by the authors in mixed diphtheritic infections. Favorable results with collargol have also been reported in the treatment of grip, typhoid fever, acute tuberculosis, and bronchopneumonia, but the authors have not been able to confirm them by their own experience. They have also been unsuccessful with it in phlebitis. Opportunity has so far not presented itself to them to try collargol in the treatment of epilepsy, in which it has been recommended. In ocular inflammations (**conjunctivitis** with **hypopyon**) Trousseau reports good results by the use of collargol ointment. The writers have at times had fair results, without being entirely convinced of its efficiency in this field. In **articular rheumatism** they prefer to first exhaust all the possibilities of sodium salicylate. In certain **subacute** cases, where this drug has failed, intravenous injections of 1 to 2 fluidrams (4 to 8 c.c.) of a 2 per cent. solution of collargol seem to cause a fall of temperature and to allay the pain; the remedy should be given a trial under such circumstances. H. Huchard and Ch. Fiesinger (Jour. des prat., Sept. 4, 1909).

Colloidal silver employed with good results in all varieties of infection. In **lobar** and **broncho-pneumonia** a 15 per cent. ointment is efficacious, provided the skin at the seat of application is previously well rubbed with a brush. In the second condition mentioned subcutaneous injections of a relatively dilute preparation, *e.g.*, 0.25 per cent. collargol, are often administered, while in the serious cases 1, 2, or even 5 per cent. preparations are given intravenously. **Pneumonia** could sometimes be arrested on the third day by this measure; in **infectious** or **rheumatic endocarditis**, in **pyemia**, and in grave **diphtheria** excellent results were also obtained. In infectious conditions with intestinal localization, the silver is given either by mouth, with coffee, syrup, or a flavored elixir, in daily doses of 0.2 to 0.4 Gm. (3 to 6 grains), or in enemas, from 0.4 to 1 Gm. (6 to 15 grains). **Dysentery** and **paratyphoid fever** sometimes yield rapidly to the enemas, while in **typhoid** the duration of the fever seems to be shortened. A. Netter (Presse médicale, Jan. 8, 1913).

Small intravenous injections of collargol are recommended by the writer in infective diseases. The strength should not exceed 1 per cent. and in the case of children 0.5 per cent. He has used it in 143 cases of different types: appendicitis, peritonitis, gonorrhea, pneumonia, etc. Good results are obtained when collargol is injected in the early stages. Gellhaus (Münch. med. Woch., lxxiii, 191, 1916). S.

**COLLODION** is a clear, syrupy fluid made by dissolving 4 parts of pyroxylin (gun-cotton) in 75 parts of ether and 25 parts of alcohol. When painted on a surface the ether evaporates, leaving a coating of pyroxylin, which is adherent and tends to contract. It should be kept in tightly corked, glass-stoppered bottles, away from lights and fires.

**PREPARATIONS AND DOSE.**—All of the preparations of collodion are used externally.

*Collodium*, U. S. P. (collodion).

*Collodium cantharidatum*, U. S. P. (cantharidal collodion, blistering collodion), is prepared by mixing 60 parts of cantharides with acetone and glacial acetic acid, percolating, reducing by distillation to 15 parts, and adding 85 parts of flexible collodion.

*Collodium flexile*, U. S. P. (flexible collodion), is composed of 95 parts collodion, 2 parts Camphor, and 3 parts castor oil. It has the advantage over the ordinary form of not cracking.

*Collodium stypticum*, N. F. (styptic collodion), is made by dissolving 20 parts of tannic acid in flexible collodion, enough to make 100 parts.

Various drugs, as iodine, iodoform, chrysarobin, cocaine hydrochloride, and salol, are often added to plain collodion for different therapeutic purposes.

**PHYSIOLOGICAL ACTION.**—Collodion is used as a protective, hemostatic, and blister, sometimes causing irritation and pain.

**THERAPEUTICS.**—Collodion is used to seal small wounds and cover excoriated surfaces. It is particularly useful in scalp wounds, as it holds together the edges of the wound, excludes the air, and a bandage is not needed. Because of its contracting properties collodion is used in **boils** and **styes**, and applied to the papules in **small-pox** to prevent pitting. It is also used in **erysipelas**, superficial **burns**, and **herpes zoster**. Because of the pressure produced, it may be used in **umbilical hernia**, **varicocele**, and **spina bifida**.

French surgeons have used collodion advantageously in the treatment of **tuberculous peritonitis**, painting it over the entire abdomen. Styptic collodion may be used in **cracked nipples** and small wounds where an astringent action is wanted. Iodine and iodoform are sometimes dissolved in collodion and painted on **gouty** or **rheumatic joints**, and iodized collodion (5 per cent. iodine in flexible collodion) is said to be of value in **chilblains**. H.

## COLLODION, BLISTERING.

See CANTHARIDES.

## COLOBOMA LENTIS. See

CRYSTALLINE LENS.

## COLOBOMA OF CHOROID.

See IRIS, CILIARY BODY, AND CHOROID.

## COLOBOMA OF IRIS. See

IRIS, CILIARY BODY, AND CHOROID.

**COLOCYNTH**, also known as "bitter apple" or "bitter cucumber," is the peeled and dried fruit of *Citrullus colocynthis*, a plant grown in nearly all parts of the world. Colocynth has a white or yellowish-white color, and is light and spongy in character. It may be separated longitudinally into three parts, and near the outer surface of each many small, oval, compressed seeds having a whitish or light-brown color are found. These seeds are always removed from the pulp in the preparation of the drug. It has a slight odor and an intensely bitter taste. Colocynth contains *colocynthin*, *citrullin*, and *colocynthitin*. The first is considered the active principle and is a glucosid, either amorphous or crystalline. It is an intensely bitter substance, readily soluble in water, alcohol, and ether, and decomposed by acids into glucose and a resin, *colocynthein*.

The so-called "colocynthin" and "colocynthitin," as well as the other products obtained from colocynth by previous investigators, to which specific names have been attached, consist of mixtures of a very indefinite character, and the amount of glucosidic substance contained in the fruit is extremely small. The purgative action of colocynth is due to at least two principles, one of which is alkaloidal, although a very weak base apparently incapable of forming any crystalline salts, while the other source of activity is represented by some non-basic principle or principles contained in both the ether and chloroform extracts of the resin. F. B. Power and C. W. Moore (Jour. of the Chemical Soc., Feb., 1910).

**PREPARATIONS AND DOSE.**—*Colocynthis*, U. S. P. (colocynth), may be given in 1-grain (0.065 Gm.) doses.

*Extractum colocynthidis*, U. S. P. (extract of colocynth), is prepared by maceration with alcohol, expression, and strain-

ing, followed by percolation and evaporation. Dose,  $\frac{1}{2}$  grain (0.03 Gm.).

*Extractum colocynthidis compositum*, U. S. P. (compound extract of colocynth), contains 160 parts of extract of colocynth, 500 parts of purified aloes, 60 parts of cardamom, 140 parts resin of scammony, 140 parts of soap, and 100 parts of alcohol. This is melted, strained, and reduced to a fine powder. Dose, 4 grains (0.25 Gm.).

*Pilula cathartica composita*, U. S. P. (compound cathartic pills), contain 60 parts of calomel, 80 parts of compound extract of colocynth, 20 parts of resin of jalap, 15 parts of gamboge, and diluted alcohol, a sufficient quantity. Dose, 2 pills.

*Pilula cathartica vegetabiles*, N. F. IV, (vegetable cathartic pills), contain 60 parts of compound extract of colocynth, 30 parts of extract of hyoscyamus, 26 parts of extract of jalap, 15 parts of extract of leptandra, 15 parts of resin of podophyllum, 8 parts of oil of peppermint, and diluted alcohol, a sufficient quantity. Dose, 2 pills.

**PHYSIOLOGICAL ACTION.**—Externally, colocynthin is an irritant to mucous membranes, especially those of the eye, nose, and throat. Internally, small doses of colocynth act as a simple bitter, increase the secretions, and improve the appetite. Larger doses act as a powerful drastic and hydragogue cathartic, increasing the biliary and intestinal secretions. The griping tendency may be overcome by combining the drug with aromatics or small doses of hyoscyamus or belladonna. Colocynth seems to have a distinct diuretic action, and colocynthin is said to excite renal irritation or inflammation when given either hypodermically or by mouth. Colocynth acts indirectly as an emmenagogue.

**POISONING.**—Overdoses of colocynth cause gastrointestinal irritation and inflammation, griping, purging, and bloody stools. Excessively large doses may cause convulsions and even death.

Case of colocynth poisoning in a woman of 29 years. An improvised tincture of an entire colocynth "apple" in 4 ounces (120 c.c.) of gin was swallowed as an abortifacient. One hour later there were faintness, vomit-

ing, and epigastric pain. A watery, large, blood-tinged stool followed, and a little later a convulsion. Temperature normal; pulse 62, weak, and irregular. The patient was frequently delirious. Emesis occurred about thirty times in the first twenty-four hours. There were 2 convulsions and 4 blood-stained stools. Next day extreme prostration and epigastric pain were noted, and ten evacuations from the bowels; also three attacks of vomiting. Prostration and epigastric pain marked. For five days the dejecta numbered at least 9 daily, and were regularly blood-tinged. There was no febrile movement. Treatment: **Morphine sulphate**,  $\frac{1}{4}$  grain (0.016 Gm.), and **atropine sulphate**,  $\frac{1}{150}$  grain (0.0004 Gm.), hypodermically, twice on first and second days, once on third day; also **bismuth subnitrate**, **cocaine hydrochloride**, and **lime water** in mixture (amounts not stated) for three days. Thereafter bismuth subnitrate alone was given every three hours in 15-grain (1 Gm.) doses. **Fomentations** to epigastrium and abdomen gave much relief. Forty grains (2.6 Gm.) of colocynth have proved fatal, and recovery has followed the taking of 3 drams (12 Gm.). In this instance between 3 and 4 drams (12 and 16 Gm.) were swallowed. Apart from the intense gastroenteritis, the main toxic effect was depression of the circulatory and central nervous systems. Abortion did not result. W. E. Jennings (N. Y. Med. Jour., Sept. 2, 1899).

**Treatment of Poisoning.**—If the patient is seen shortly after the drug has been taken, emetics, as **zinc sulphate**, or **apomorphine**, followed by **demulcents** and **morphine**, are indicated, with **stimulants** in the event of collapse.

**THERAPEUTICS.**—Colocynth is a most useful drastic cathartic, but should be given in carefully regulated doses and properly combined with other remedies. For the relief of **constipation** the compound extract or compound cathartic pill may be given. The compound extract combined with extract of **physostigma** is satisfactory in some cases of habitual con-

stipation. Colocynth given in combination with iron is useful in the treatment of **chlorosis**. This drug may be of benefit as a derivative in the various forms of **neuralgia**, in chronic **edema** of serous cavities, and in **cerebral congestion**. It is also of value in **melancholia** and **hypochondriasis** in which there is autointoxication due to sluggishness of the intestine and fecal accumulations. Colocynth is contraindicated in all inflammatory conditions of the intestinal tract. It should be administered with caution during pregnancy.

H.

### COLOR-BLINDNESS, OR ACHROMATOPSIA.—

When the innumerable shades and tones of objective color existing between the red and the violet ends of the solar spectrum are compared with the physiological or subjective color-spectrum of a normal human visual apparatus, it will be at once realized that every person possesses a subnormal degree of color-perception. Lockyer tells us that Chevreul was able to distinguish and designate 14,420 different tones of color. Here was a man who, by education, caused his color-seeing organ to recognize such a great number of changes that he is quoted as remarkably acute; and yet we see how low his power of color-perception falls when we think of the millions of differences of color that might be perceived.

A single difference of vibrating movement in ether waves makes a change in natural color, and each such change gives a different degree of sensory impulse, and, hence, a difference in visible color. It is not the arbitrary subjective nomenclature of the solar color-spectrum, for example, into its well-known seven integral parts (violet, indigo, blue, green, yellow, orange, and red), that is necessary. It is not the unscientific

and, at times, nonsensical anatomical construction of the color-perceiving apparatus into adapted component parts that is obligatory. Gross specialization of receiving tip, of transmitting fiber, and of discharging molecule, as is seen in the many fanciful and even farcical theories which are in common use even at the present time is not obligatory.

Each difference of color-wave acts in its pure idiocratic way upon one and the same receiving anatomical tip; each tip receives such an impression, and, in conformance with its special ability, transforms the impression into an equivalent active energy; and each transmitting fiber carries the transferred energy to its anatomical representatives in the cerebral cortex, in which place it is interpreted by a series of associated sensorial acts.

As with the individual neurones, so with the composite series. Visual apparatuses are just as unlike in construction and physiological action as any of the other sensory structures.

An inability to recognize delicate differences of color, which is simply the result of the lack of color education, must not be confounded with this normal limitation of color-perception. Racial peculiarities of life, sexual differences, constant association with color-distinctions, must all play their important parts in this question. Color-differentiation as a means of existence, color-selection as a daily exercise, and color-distinction as an avocation,—all bring into sensible activity elements of color-seeing which ordinarily remain dormant and unused. To assert that a person whose eyes are not trained to detect delicate differences of color has a

physical type of subnormal color-perception would be about as foolish as to declare that an uneducated and unused muscle is incapable of proper action if repeated correct stimuli be applied to it.

The following points should be remembered in examination for color-blindness: 1. Most color-blind persons make mistakes with certain colors, but are correct with regard to others. 2. The color-blind name colors in accordance with their color-perception, and thus show definitely to which class they belong. 3. Colors may be changed to the color-blind while leaving them unaltered to the normal-sighted. 4. The phenomena of simultaneous and successive contrast are much more marked for the color-blind than for the normal-sighted. 5. Many color-blind match correctly, but name the principal colors wrongly. 6. Many color-blind recognize colors easily when they are close to them or the surface is large, but fail to distinguish between them when they are at a distance or the image on the retina is small. 7. The color-blind are more dependent upon luminosity than the normal-sighted, and are liable to mistake a change in luminosity for a change of color. 8. The color-blind find special difficulty with faint and dim colors. 9. The color-blind who have shortening of the red end of the spectrum cannot see reds reflecting or transmitting only rays corresponding to the shortened portion. 10. The color-blind find more difficulty in comparing colors when different materials are used than when the colored objects are all of the same nature. 11. Most color-blind find more difficulty with transmitted than with reflected light. 12. The color-blind have a defective memory for colors. 13. Colors may be changed to the normal-sighted while leaving them unchanged to the color-blind. 14. The color-blind may have a sense of luminosity similar to that of the normal-sighted. 15. The dichromics

distinguish between the colors of the normal-sighted which are included in one of theirs by their relative luminosity and the difference of a saturation which is apparent to them. Edridge-Green (*Lancet*, Feb. 11, 1911).

The examination of red-green blindness proves whether or not a lesion exists in the visual nerve-tract. A disturbance of the color-sense is the first sign of functional visual disturbance; this can be demonstrated even before any diminution in vision has taken place, and when a diminution in vision can be proven it is difficult to decide in the beginning whether it is due to an anomaly of refraction or to opacities of the refraction media. Kölner (*Wiener klin. Rundschau*, June 4, 1911).

Based upon the fact that a constantly increasing use of an organ from generation to generation must render it stronger in power and more extended in its action, it is not presumptuous to assert that, if this be so (which daily experience and history teach us), there will be a time when the color-seeing power of the human species will far exceed anything dreamt of at present. Then, however, arise the at-present-unanswerable questions: Shall the human visual apparatus ever become perfect organs for color-seeing? Will there not be a something more for it to conquer? Will there not be a search for the unobtainable?

As it is true that there is an average proportion of 1 out of every 5 male subjects and 1 out of every 20 female subjects who have a subnormal variation from the gross mental standard of seven pure visible colors with a certain unknown quantity of correlated tones and shades, it remains only to find those cases in which such a defect can be determined: this is best and most easily accomplished by

some modification of Wilson's wool method.

**TESTS.**—For the detection of defects in the color-sense wools of various hues are made use of, the method devised by Holmgren being the one in most general use. A number of skeins of wool comprising different shades of green, red, and their confusion colors (gray and brown) are placed before the patient, who is given a skein of green-colored wool. This is called the test skein and he is required to pick from the pile of wools in front of him the skeins of the same *color*, not the same *shade*, as the one he holds in his hand. If there is any defect in his color-vision the patient will select a number of the confusion colors (chiefly grays), with perhaps some green tints. If he accurately chooses all greens the investigation need proceed no further; he has normal color-sense—is not color-blind. If, however, he fails in this he is now given a rose-colored skein and again told to choose skeins of that color. He is now likely to match the rose with browns, purples, dark grays, or even greens. Finally he is given a deep-red skein, when he will choose the dark browns and greens. The great majority of color-blind people are defective in red and green and are said to have red-green blindness, although all varieties, from simple green to total color-blindness, exist. With this test it is almost impossible for one who is color-blind to escape detection. Congenital color-blindness is more common in men than in women, being in the proportion of about 4 per cent. in the former and about 1 per cent. in the latter. The defect cannot be overcome, but fre-

quently a color-blind individual is able to distinguish to a certain degree the various colors, although he does not see them as such. Acquired color-blindness may be due to some organic changes in the optic nerve or visual centers, as seen in toxic amblyopia, hysteria, optic nerve atrophy, and other conditions (C. A. Wood and T. A. Woodruff).

Study of color perception in 25 "normal" persons. Those found with defective color perception were surprisingly numerous, the anomalies ranging from slightly abnormal perception to total lack of perception—color-blindness. In some cases part of the color had dropped out of view although what was left was seen in its true tint. This is a comparatively common defect, according to the writer. Even if some test should yet be found applicable to all cases, it would still be a question whether railroad signals by colors had not better be abandoned, as being far from dependable. B. Malling (Norsk Mag. f. Laegevid., Jan., 1918).

According to Eldridge-Green, who has for years studied color-blindness, the wool test has proved a failure, although it is still used by the British Board of Trade. He proved that many dangerously color-blind men had passed that test, and his experience has been confirmed by others. Conversely, of those rejected by the wool test and who appealed, over 53 per cent. were found to be normal-sighted. The defects of the method were many. It is difficult to obtain correctly colored wools. A further difficulty is found in obtaining duplicates of these wools. If two colors look alike they do not have necessarily the same composition; if the dyes used are different, the colors probably differ in composition. Fur-

ther, when a good set of wools has been secured, the colors are liable to fade, some more rapidly than others. This prevents the results of examinations made with that set from being uniform. Then the wools, or some of them, very soon become soiled. The greens which it is necessary to pick out get more soiled than the others and so afford a mark of distinction to the color-blind, who, not being confused by the striking differences of color, noticed minutiae of this kind. In testing a number of persons the color-blind ones try to find some distinguishing mark in wools selected by others. Color-blind people may distinguish between brown and green by the touch, but not by sight. The relative luminosity of the colors of wools is also considerable and forms a distinguishing point to the color-blind. A pure green is one of the worst possible colors to choose for a first test. If the blue-green is removed, color-blind persons easily pass through the whole list and are not detected. The test is theoretical rather than practical, the main object of testing being lost sight of. Thus, a man who put a confusion color with a green wool could not tell a red from a green light, and when he had done so it was still to be decided whether he had been judging more by shade than color. Moreover, it is possible to instruct a red-green color-blind person so as to enable him to pass through the test with ease.

As a result of these observations Eldridge-Green invented a lantern which, as emphasized by W. M. Beaumont recently (1912), presents many advantages over Holmgren's yarn in the testing of color-vision. The advantages of the lantern are

that it is simpler to apply; the colors do not fade or get soiled by time or use; the lantern is a method of testing which resembles the actual signals in use by land and sea, and the obscurity produced by distance, fog, mist, or rain can be closely imitated. The two signal colors are red and green. The lantern can be arranged to show the red as seen on a foggy day; some color-blind men, while recognizing the red as red under ordinary circumstances, will call it green when it is modified by fog. By varying the size of the diaphragm aperture one can represent the bull's eye signal lantern as seen at 600, 800, or 1000 yards.

A seaman who can infallibly and in all conditions of weather identify a port light and a starboard light—that is, a green and a red light—is quite safe for purposes of navigation. It is a question as to whether a given man can determine three different lights, namely red, green, and clear. Supposing a candidate is required to distinguish three different notes as to pitch, such as a high note, a low note, and one about half-way between the two, would it be reasonable to ask him to have the knowledge of tone which is requisite to tune a violin? That is practically what is demanded of the modern sea officer in relation to color. Freeland Fergus (*Glasgow Med. Jour.*, June, 1910).

It is of great importance to divide the color-blind into the dangerously color-blind and the harmlessly color-blind. This may be done satisfactorily and expeditiously with the Eldridge-Green lantern after gaining an understanding of the principles of the test employed. The Jennings test results in the rejection of a large percentage of subjects who should be accepted, especially among the more intelligent, but it possesses certain lines of examination where great accuracy and classification of color defects are not essential. Collins (*Amer. Jour. Med. Sci.*, Feb., 1919).



A congenital case of total color-blindness is rare, and more so is the acquired form. A one-sided lesion in the color-center is occasionally met with. It is well recognized that there are symptoms which point to intracranial pressure which precede papilledema, and among these are changes in the recognition of color. The importance of these prepapilledematous symptoms lies in the fact that the tendency of present-day surgery is in the direction of early decompression operations.

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**COMA, DIABETIC.** See DIABETES MELLITUS.

**COMPRESSED AIR, DISORDERS DUE TO.**—The diseases which come under this head are Caisson Disease and Divers' Paralysis.

#### CAISSON DISEASE.

This term has been given to the morbid effects of compressed air produced upon individuals who, employed in the construction of subaqueous tunnels, piers for bridges, heavy buildings, etc., work in caissons in which the air is compressed for technical purposes. The disease manifests itself only, however, when the pressure reaches a certain limit, about fifteen pounds, or two atmospheres, in addition to the ordinary atmospheric pressure (L. M. Ryan). The highest pressure in which work is done is about fifty-five pounds.

**SYMPTOMS.**—Pain in the ears and sinuses, especially if catarrh of the Eustachian tube is present, and some deafness while being compressed or decompressed, is experienced; some vertigo may also occur and the voice becomes metallic or assumes a nasal twang. Although the pulse is accelerated at first, it soon becomes normal; the breathing, though somewhat shallow, is also normal. General oxidation is enhanced, as shown by increased appetite, rapid hair growth, in-

creased vigor, etc., but, on the whole, the caisson worker experiences no serious discomfort.

Gas from the right heart of a man who had died following 8 hours' exposure to +30 pounds pressure, yielded nitrogen 80 per cent., CO<sub>2</sub> 20 per cent., which percentages are in accord with analyses made in animal experiments by various writers. Erdman (*Amer. Jour. Med. Sci.*, Apr., 1913).

Caisson sickness and caisson paralysis may be classed as an accidental injury, coincident to a lowered bodily metabolism and preceded by a certain amount of shock, due to mental anxiety. This is borne out by a number of his cases, where illness occurred the first shift that the patient worked. Further, in which from whatever cause, there is an engorgement and a certain amount of stasis of the blood in the larger vessels of the trunk. Let this condition be augmented by an excess of nitrogen gas in the blood-stream, the pressure becomes still greater and the traumatism occurs. Sewall (*Journal-Lancet*, May 15, 1915).

It is during or after the process of gradual decompression incident upon his return to normal air pressure that the evil effects appear. These, apart from a few transitory symptoms, defective vision, tinnitus, mental confusion, and excitement, may be divided into two classes: spinal and cerebral.

**Spinal Type.**—This type is that most commonly witnessed. In, or on emerging from, the decompression chamber to which the men pass from the air-lock to be "decompressed" more or less severe pains in the muscles of the limbs and joints (often termed "bends" by the caisson workers), sometimes lasting weeks, with paralysis of the bladder and rectum, occur. The pulse becomes hard and rapid, the patient is pale and bathed in perspiration, and the reflexes are somewhat enfeebled. Abdominal pain is sometimes complained of and may be very severe. In marked cases, paralysis of the limbs with loss of sensation may come on more or less suddenly. It is usually not permanent, though it may

last months. The reflexes here may be absent, the pulse rapid, the pupils dilated, and the face pale or somewhat cyanotic. The abdominal pain becomes not only more severe, but is accompanied by a sensation of constriction and burning recalling that of herpes zoster. These phenomena, due to intraspinal hemorrhage, may gradually disappear or become increasingly serious and ultimately end in death. Occasional numbness may occur in otherwise apparently well subjects.

**Cerebral Type.**—This type, which occurs in a small proportion of cases, is attended by phenomena which suggest passive vasodilation of the cerebral vessels, with ischemia of the superficial tissues. The cerebral symptoms may only be slight, giving rise to nausea and vomiting, tinnitus, vertigo, flashes of light, headache, acceleration of the pulse, free perspiration, and pallor, the superficial ischemia being shown, moreover, by superficial hypothermia. In severe cases the facial pallor is succeeded by cyanosis, the patient is more or less deeply comatose, sometimes slightly delirious, his vision blurred, the respiration and pulse very weak and rapid, and the surface cold and clammy. Hemiplegia may also occur in this type, but is not complete, the patient retaining some power of motion. The paresis may affect all the extremities. In fatal cases the depressive symptoms become steadily worse, all vital functions being arrested through circulatory failure. There may also be frothing at the mouth, convulsive movements, and epistaxis. A fatal issue usually occurs in such cases.

Analysis of 300 cases showed that the following symptoms occurred in the order of frequency given below: Myalgia, or severe pain in the muscles, and especially in the muscles of the back, but also in the muscles of the extremities, seems to be a uniform accompaniment of the disease. It occurred in 105 of the 310 cases analyzed. The second most frequent symptom is an affection of the ears, producing symptoms comparable to Ménière's disease; vertigo, vomiting, intense prostration, tinnitus aurium, and deafness. These symptoms occurred in 68 cases.

Pain in the joints, classed together as arthralgias, occurred in 60 cases, in many of them being attended also by myalgia. It seems probable that in these cases there has been a sudden effusion of fluid into the joints, stretching the capsules of the joints without any acute inflammatory condition, and in proof of this the frequency of swelling without heat or redness can be cited. In 26 cases acute paraplegia developed. Monoplegia was observed in 17 cases, cerebral in type rather than spinal, and undoubtedly due to localized areas of softening, or to malnutrition in the cortex produced by bubbles of air in the veins of the brain. Symptoms of intense vertigo of cerebral nature, undoubtedly due to emboli in the cerebellum, were noted in 14 cases. These resembled in many respects the symptoms of Ménière's disease, already mentioned, but were followed by paralysis of some of the cranial nerves, indicating that the origin of the symptoms was not in the ear. The seventh most frequent set of symptoms were classed together as asphyxia, the patients showing all the signs of faintness, with irregular heart action; 13 patients suffered from this symptom.

Aphasia has been observed in a number of the cases. Recoveries have also been recorded in many cases in which the symptoms were largely cerebral. Thus, in cases presenting the phenomena of acute transitory mania, in other cases presenting symptoms of hemiplegia, and in other cases presenting the symptoms of various types of aphasia, temporary deafness, and temporary blindness, as well as in those very numerous cases in which peripheral disturbances of the auditory nerve had been produced by lesions of the inner or middle ear, recoveries have been recorded. It is evident, therefore, that in the cases of apoplexy or of paraplegia occurring with caisson disease the prognosis is very different from that of the usual case. Starr (Med. Record, June 19, 1909).

The symptoms may present the picture of an acute myelitis and cerebral symptoms follow.

**PATHOLOGY.**—The fact that the early symptoms are relieved if the patient at once returns to the compression chamber and is "recompressed" indicates that the morbid phenomena are due to the abrupt transition from an atmosphere of high density to one relatively rarefied. As to the ears, the morbid symptoms occur only if the workman does not, by the method of Valsalva or repeated deglutition, force air into the Eustachian tubes and thus equalize the pressure on both sides of the membrana tympani. Otherwise the latter and the ossicles are compressed from the exterior and may show congestion and even varicose veins (Berruyer). The membrane may even rupture and lead to hemorrhage and perforation if the compression—or decompression—is carried out too rapidly.

The gravest ear disorder is rupture of the membrane itself, which accident is accompanied by a noise like that of a cannon firing and often followed by syncopal attacks. Rupture of the membrane may occur during the stage of compression and results from a too low pressure of air in the tympanum, the result of pharyngeal, nasal, or Eustachian tube obstruction. Rupture may also occur during decompression when this is carried out too rapidly. Maurice Philip (*Gaz. hebdomadaire des sciences médicales*, May 5, 1907).

In a study of the effect on the blood of work in caissons, the writer found a form of anemia characterized by a decrease in the red blood cells, hemoglobin, and often the white cells. The morphological changes in the cellular elements consisted in an increase of microcytes, a decrease in the polymorphonuclears, and an increase in the lymphocytes and eosinophiles. Occasionally, hyperleucocytosis was observed. With cessation of the work the blood returned to normal in 4 to 6 weeks. Solovtsoff (*Roussky Vrach*, June 7, 1914).

The prevailing view is that the disease is due to the excess of air, both oxygen

and nitrogen, forced into the blood on its passage through the lungs, by the excessive pressure. When decompression is carried out slowly, *i.e.*, very gradually, the excess of these gases in solution in the blood escapes from the pulmonary alveoli and is eliminated during expiration, the blood-pressure being also caused to resume the normal. If, on the other hand, decompression be carried out abruptly, the process of elimination is interfered with and air embolism into the brain and spinal cord occurs, while the blood-pressure fails to adjust itself to the diminished air-pressure. As a result there occurs a mechanical congestion of all tissues, muscles, joints, brain, spinal cord, etc., with results corresponding with the degree of hyperemia produced and sufficient in severe cases to produce rupture of the vessels and hemorrhage. Besides this general hyperemia a multitude of minute bubbles composed chiefly of nitrogen are forced into the blood and carried by it to all tissues.

The characteristic pains and rigidity were, in a personal case, due largely to the irritative nature of the cord lesions. The relief of urinary retention by the administration of **pituitary extract** is of special importance for the reason that cystitis is a most serious complication in the disease. The onset of recovery following **lumbar puncture** is also suggestive in the pathological sense. Keyser (*Cleveland Med. Jour.*, Apr., 1916).

A workman, new at the task, experienced the third day intense pain in his left thigh with other symptoms of caisson disease, followed by a vast eschar along the course of the deep gluteal artery which proved to be due to bubbles of gas large enough to obstruct it. Jean and Viguier (*Bull. de l'Acad. de méd.*, Paris, Oct. 22, 1918). Dilatation of the right heart and air emboli therein are also common. Any degenerative lesion of the heart or blood-vessels obviously increases this danger.

The writer and Alfred Parkin subjected frogs to extremely high pressures and after a time suddenly decompressed some of them. The web of a frog's foot was drawn over

the inside of the glass window of the compressed-air chamber and by means of the microscope and electric-light illumination we could watch the circulation of the blood in the frog's capillary. During compression the circulation proceeded quite naturally, but after sudden decompression, while the circulation seemed to go on apparently unchanged, by degrees the rate of the blood-flow diminished and gradually ceased, preceded by a slight to-and-fro movement. All at once a bubble or two of air would appear in the capillaries and, these running together, formed a large embolus inside the vessel. Occasionally air-bubbles appeared in the tissues external to the blood-vessels and were due sometimes to rupture of the capillaries or to desaturation of the tissues. It is the presence of gaseous emboli in blood-vessels, the accompanying stagnation of the circulation, and the occasional rupture of small blood-vessels with hemorrhage which are the pathological lesions present in most cases of compressed-air illness. It is the bubbles of nitrogen gas in the small blood-vessels of the brain and medulla and the presence of air-spaces in the cerebral tissue which explain the sudden death of divers and caisson workers after decompression; also the presence of similar lesions in the lower part of the spinal cord which explains the paralysis of the lower limbs and, when present in the muscles and around the joints, the severe pains known as "bends." In opening the bodies of frogs, mice, and rats which had died shortly after decompression bubbles of air can be seen escaping from the heart when that organ is cut into; also from the liver and the subcutaneous tissues. The bubbling of gas in the blood and tissues of the body after sudden decompression is aptly compared with the effervescence which occurs in a bottle of soda water on removal of the cork, and, in a word, is the pathology of caisson disease. Sir Thomas Oliver (Lancet, Jan. 30, 1909).

In subaqueous tunnels the loss of air by leakage is sufficient to maintain perfect ventilation, and, therefore, carbon dioxide, carbon monoxide, and other gases do not accumulate in sufficient quantities to be considered as a possible etiological factor in the causation of compressed-air illness. The direct cause of this condition is the presence of air-bubbles in the circulation; these gas-bubbles consist of nitrogen, carbon dioxide, and oxygen, of which nitrogen is in excess, for the reason that this gas is the chief constituent of the atmosphere, and also does not combine with any of the body tissues. New workers are most susceptible to this disease until the body accommodates itself to this entirely abnormal condition of high air-pressure, and, therefore, it is of the utmost importance that only young, healthy men should be allowed to do this work. New workers should, when feasible, be started in low pressures, from which in the course of four or five days they may graduate to become, as they are called, "high-pressure men." J. E. McWhorter (Amer. Jour. Med. Sci., March, 1910).

It is not the exposure to increased atmospheric pressure that causes the condition known as caisson disease, but it is decompression that causes the trouble. There is no risk in going into or staying in a caisson; "*on ne paie qu'en sortant.*" The cause of the illness was suggested by Hoppe-Seyler and made clear by Paul Bert, whose experiments on animals showed that nitrogen is dissolved in the blood and in the tissue fluids in proportion to the pressure of the air. The dissolved gas on too rapid decompression bubbles off and effervesces in the blood of animal or man. The bubbles, by blocking up the capillaries and cutting off the blood-supply here and there, produce the symptoms. Exposure to high atmospheric pressure has no ill effect until the pressure becomes so great that the partial pressure or concentration of oxygen acts as a tissue poison.

The illness which occurs on decompression is prevented by making the period of decompression sufficiently slow to allow time for the dissolved nitrogen to escape from the lungs. L. E. Hill (Brit. Med. Jour., Feb. 17, 1912).

**TREATMENT.**—The only specific for caisson disease is **recompression** at the earliest possible moment. In medical quarters connected with, or readily accessible to, the place where workmen are exposed to compressed air, "hospital locks" made of boiler iron, are available in which the sufferer can at once be given the benefit of the process.

It is, indeed, gratifying and little short of miraculous to see a man completely paralyzed from his waist down or bent double with excruciating pains in his abdomen or legs placed in the lock, the pressure turned on, and long before the tunnel pressure is reached the paralytic walking about and the sufferer smiling. In treating the patients, the pressure is rapidly raised to tunnel pressure, and at once very slow decompression is instituted at the rate of two minutes to one pound. Frequently after this treatment the pains return and recompression once, twice, or more times is advisable. In 1343 cases of 1419 patients treated by recompression, complete relief being afforded 869, or 64 per cent., 50 per cent. were completely relieved by one **recompression**, 28 per cent. were so much relieved as to be able to go home and carry out therapeutic measures, and only 8 per cent. failed to get relief at all. S. Erdman (Jour. Amer. Med. Assoc., Nov. 16, 1907).

When the patient is suffering from a mild type of the disorder and if seen soon after the onset of the symptoms, the relief experienced is striking, the pains in the extremities, abdomen, etc., disappearing long before the pressure to which he is subjected during working hours has been reached. The latter pressure having been attained and maintained for five or ten minutes, the patient is then decom-

pressed, but *very slowly*, one pound in four minutes, thus occupying one hour for a pressure of fifteen pounds—while simultaneously pumping a certain amount of fresh air into the lock. When relief is experienced from the pains of an ordinary attack Pelton (Amer. Jour. Med. Sci., March, 1907) directs the patient to move about the lock and to **exercise** and rub the affected part with a counterirritant ointment (see below). In most of the mild cases the patient leaves the lock wholly relieved, but if there is a return of the pain recompression is advisable, the pressure being allowed to ascend until the pain disappears, when slow decompression is instituted as before. A third or even a fourth recompression may be employed if necessary, but usually the relief experienced from these subsequent treatments is temporary and slight in character. It is wise, if there is still continuation of the pain after the patient has been sufficiently recompressed, to advise thorough **rubbing of the painful part with a counterirritant ointment** or liniment. The following are suggested by Pelton:—

**R** *Capsicum oleoresin*..... 2 parts.  
*Oil of turpentine*,  
*Oil of rosemary*,  
*Camphor*,  
*Olive oil*.....of each 5 parts.  
*Petrolatum*, to make..... 100 parts.

Or,

**R** *Menthol* ..... 10 parts.  
*Methyl salicylate*..... 5 parts.  
*Chloral hydrate*..... 10 parts.  
*Lanolin*, to make..... 100 parts.

The **faradic current, high-frequency current, and vibratory massage** may prove beneficial. **Hot baths, hot-water bags**, and the **electrotherm** are very helpful adjuncts. **Ironing the painful part with a hot flat-iron**, a flannel cloth being interposed between it and the skin, is also suggested.

In the more severe cases with paralysis or coma, according to a writer of considerable experience, L. M. Ryan (New York Med. Jour., July 31, 1909), the physician enters with the patient, and as soon as the required pressure has been attained the patient is encouraged to sit up and to stand and to move his extremities. If he is able to walk he is kept up

and encouraged to walk the entire time that he is in the lock. If he is unable to walk after being recompressed, his limbs are massaged, and he is held up in the standing position, while he endeavors to flex and extend his legs. **Strychnine**, gr.  $\frac{1}{80}$  (0.0022 Gm.), hypodermically, every hour for three doses, is given, and a strong purgative—preferably of **calomel** and **jalap**—is administered. If the recompression is carried out immediately after the attack appears, we usually notice a very material benefit after the patient has been back in the lock for about fifteen or twenty minutes. As soon as he shows recovery from the paralysis the air can be gradually released, and the more slowly the pressure is reduced the more ideal will be the result. Ordinary slight cases, as stated, are decompressed at the rate of about one pound in four minutes, which would be allowing one hour for a pressure of fifteen pounds. In the more serious cases, according to Ryan, whose treatment is given here, it is not wise to allow the pressure to be reduced at a rate faster than one pound in eight or nine or even ten minutes, consuming a time of sometimes three and a half hours. If the attack appears some hours after the patient leaves the tunnel, and he cannot be immediately recompressed, by reason of his being at some distance from the medical lock, recompression will not act so rapidly, although he will usually be much benefited. Fortunately the attacks that come on some hours after the patient has left the compressed air are not usually serious. The attacks characterized by pain alone go on to spontaneous recovery at any rate. If the pains are not benefited by recompression, **morphine**, gr.  $\frac{1}{4}$  (0.016 Gm.), should be administered with **calomel** and **jalap**, of each, gr. x (0.65 Gm.), and the patient should be instructed to be on his feet and keep walking.

In cases where the paraplegia is not benefited by recompression, due to delay in being able to return the patient to the medical lock, **massage** should be carried out early and faithfully, and the patient should be encouraged to get up and try to walk, and if necessary walk supported on each side by two assistants. The assistants should manipulate the legs by

flexion and extension until the patient regains some power over them. Ryan has kept patients attempting to walk almost continuously for twenty-four hours, using assistants in relays, before any benefit was noticed. It is this part of the treatment that requires the greatest care, patience, and perseverance. Attention must be paid to the bladder and bowels. The urine should be withdrawn and the lower intestine irrigated. With returning power in his legs, he regains power over his sphincters.

A paralysis that is not immediately benefited by recompression in most cases never entirely disappears, owing to the damage done to the spinal cord, either from pressure or hemorrhage. It is usually found that one leg will recover better than the other, and the patient walks dragging one foot. The gait is more ataxic than spastic. The muscular tone is diminished, and after a few weeks the wasting of the calf and thigh muscles is marked. **Electricity** is of great benefit here, and should be supplemented by regular and faithful **massage**. In those cases of paraplegia which get progressively worse, the treatment is the same as in the cases of myelitis. Even with water beds, bed-sores and all the accompaniments of myelitis ensue. If a patient does not recover in six months it will probably prove fatal, but a patient will sometimes remain in about the same condition for two months, and then gradually get well enough to walk. These patients improve up to a certain point, but never fully recover.

In cases of the lighter cerebral variety, characterized by vertigo, nausea, and vomiting, recompression is of little avail, although it is always carried out in the hope that we may increase the tone of the blood-vessels by dissolving out any air which has remained in the vessels. **Rest** and **quiet** in a dark room with light diet are most beneficial. The attack gradually wears away, until at the end of a week the patient is on a fair road to recovery. **Catheterization of the Eustachian tubes** with inflation of the middle ear is of service as well.

Before the introduction of the hospital lock for the treatment of compressed-air

disease, the treatment consisted in the application of a strong electrical battery over the affected parts, with the internal administration of **ergot** and **strychnine**, combined with the **hot-water bath** as hot as it could be borne. Only the mild cases were much benefited, and **ergot** is not used now. Electricity is only of use when the case has become chronic, or in cases of paralysis after they have failed to respond to recompression. It is important always to keep a supply of **oxygen** on hand, but it is of doubtful benefit in severe cases and unnecessary in the mild cases.

One severe attack is sufficient to bar a man from ever working in the compressed air again. All beginners are liable to have an attack of the lighter variety, characterized by pain alone, as well as old employes who violate the rules or who remain under the pressure more than the customary time. Slight attacks should not be regarded, unless repeated often, as unfavorable to a man's return to work.

**PROPHYLAXIS.**—The defective way in which decompression is carried out by the lock tenders is the main cause of the disease. Not only should the lock tender be an expert, but he should be prevented by law from decompressing more rapidly than the safest limits would warrant. All applicants should, according to Oliver, be examined medically. Men subject to intemperance, colds in the head, deafness, lung trouble, heart disease, or albuminuria should not be allowed to work in caissons. Short and thin men stand the work better than tall, stout ones. Younger men do better than old, and the longer the shift the greater the danger.

Obesity increases the susceptibility to death from caisson disease. Obese men should never be allowed to work in compressed air, and plump men should be excluded from high-pressure caissons (*e.g.*, over + 25 pounds), or in diving more than about 10 fathoms, and at this depth the time of their exposure should be curtailed. Boycott and Damant (*Jour. of Hygiene*, Sept., 1905).

The chief factor in prophylaxis, besides slow decompression, is the proper selection of the workers. There are six groups of individuals

which it is of especial importance to exclude from the high-pressure work: (1) fat men; (2) men with heart weakness, vasomotor weakness, as hysteria and neurasthenia, or arteriosclerosis; (3) chlorosis, primary or secondary anemia; (4) persons with disease of the central nervous system; (5) edematous individuals and nephritics without edema; (6) persons with ear affections. J. Plesch (*Berl. klin. Woch.*, April 18, 1910).

Case of caisson disease in which the patient had shown spastic paraplegia for over a year. The obturator was cut and the spasticity was relieved somewhat. The man is now working, which he had not been able to do before the operation. The **Stöffel operation** is a very simple procedure, consisting in making an incision in the groin and paralyzing the adductor by cutting the obturator nerve. Taylor and Byrne (*Trans. N. Y. Acad. of Med.; Med. Rec.*, Feb. 22, 1919).

#### DIVERS' PARALYSIS.

This disease is practically the same as that described above. As studied by Zegrafidi (*Revue de médecine*, Feb. 10, 1907), in 260 cases among the sponge divers on the coast of Africa, in whom it is very common,—34 per cent. of the divers suffering from spastic paraplegia,—the disease varies from the fulminating type, where death is immediate with general emphysema and multiple hemorrhages, to mild cases in which there are only slight symptoms, soon passing off without subsequent ill effects. The great majority of the cases fall into a group intermediate between these extremes. These are all more or less acute, and terminate either in death within a period varying from a few days to several weeks or in a permanent condition of chronic spastic paraplegia. The diver on coming to the surface complains of pains in the whole body, especially the trunk; disturbances of vision and hearing, and tingling in the lower limbs, which rapidly become paralyzed. After some hours a general improvement occurs, and for fifteen to forty-five minutes the patient feels well, and may be able even to walk

about. Then the tingling returns, and paraplegia finally and definitely establishes itself. In the milder cases recovery ensues with permanent paraplegia; in the more severe the condition becomes progressively worse, until death supervenes.

Analysis of 12 fatal cases and 18 cases of permanent or temporary paralysis occurring in divers. One of the patients had seven different attacks of paralysis, the last rendering him entirely helpless. The predisposing conditions are evidently age above 45 or 50, pulmonary affections, fatigue, alcoholism, eating before going down into the water, excesses of all kinds, long-continued work, and the depth to which the diver descends, but the principal factor is the sudden change from compressed to ordinary air. If the change from the compressed to ordinary air can be made gradually, there is much less likelihood of trouble. Individuals working in compressed air should be on the lookout for special pains and slight signs of paralysis and should accept them as a warning. The writer suggests rigorous administrative inspection of diving bells to see that they are in good working order at all times. Boinet (Bull. de l'Acad. de Méd., vol. lxx, No. 26, 1906).

**PATHOLOGY.**—The spinal lesions were those of a typical myelitis in all the cases examined *post mortem* by Zegrafidi. As the result of the liberation of gases in the blood, numerous emboli occur in the arteries of the cord, and these produce ischemic foci, which undergo speedy softening and necrosis. In severe attacks hemorrhages also occur in the cord. These foci become inflamed, and a true myelitis develops, which follows a typical course. The early symptoms are complicated by cerebral disturbances caused by bubbles of air in the cerebral vessels, and much of the early pain is due to direct tearing of nerves by distention of the vessels with air. These bubbles are again absorbed, and with their absorption comes the interval of apparent recovery, which is cut short by the congestion arising as the first stage of the developing myelitis.

In one of Zegrafidi's autopsies the cerebral vessels were found thirty-six days after the onset of the disease to be full of air-bubbles, which could be moved along the vessels with the finger.

Death is almost certainly due to embolism and blocking of cerebral or pulmonary vessels by the bubbles of nitrogen set free in the circulation by too rapid decompression. Nausea and vomiting occur directly on the diver coming to the surface, and are usually due to a heavy meal just previous to descent. Mummery (Brit. Med. Jour., June 27, 1908).

**TREATMENT.**—Very gradual decompression, similar to that employed in caisson disease, is also the only specific treatment of divers' paralysis when at all amenable to treatment. All the other measures indicated under Caisson Disease are also applicable here. S.

**CONCUSSION OF THE BRAIN.** See HEAD AND BRAIN, DISEASES OF.

**CONDURANGO.**—This is the bark of *Gonolobus condurango*, a vine growing in S. America. It is separated from the tree and dried in the sun. It has a smooth external surface, and a gray color. Condurango contains a yellow resin, tannin, and two glucosids. The root contains 7 per cent. of *condurangin*, a glucosid which causes toxic symptoms when given hypodermically. The drug is not official.

**PREPARATIONS AND DOSE.**—Condurango may be given in the form of the *fluidextract*, (N. F.), 1 fluidram (4 c.c.); the *wine*, dose 4 fluidrams (16 c.c.), and the *decoction*, dose 4 fluidrams (16 c.c.). The decoction is made with 8 parts of water to 1 part of the bark.

**PHYSIOLOGICAL ACTION.**—The effect of condurango is said to be due to the resin. Small doses may be used as an astringent bitter, stomachic tonic, and sedative. It is also said to act as a diaphoretic and diuretic.

Large doses produce, in dogs, ataxia and inco-ordination, increased motor activity, and convulsions. Large doses, in man, act chiefly upon the brain, causing vertigo, disturbed vision, and increased activity of the circulation.



**THERAPEUTICS.**—Condurango was first used in **gastric carcinoma** and **gastric ulcer**, as it was thought to cure these conditions. It is now known that the drug has no effect on these diseases, but that it does allay the pain and digestive disorders which accompany them. In South America it is used as an alterative in **sypthilia**.

The writer finds, in both the condurango leaves from Ecuador and the kawar root from the Transvaal, ethereal oils that are very similar in their characteristics. Both plants come from their native places recommended as cures for **cancer**, both belong to the same family, and the chemical composition of the drugs obtained from the two bears an extremely close resemblance. Bohm (Münch. med. Woch., Aug. 25, 1908). H.

**CONIUM** is the fully grown but unripe fruit of *Conium maculatum*, carefully dried and preserved. It is unfit for use if kept for two years. It has a characteristic acrid taste and a slight odor, which becomes strong, disagreeable, and mouse-like when the drug is triturated with potassium hydroxide.

Conium contains an active principle, *coniine*, which is an oily, colorless, volatile alkaloid having a disagreeable odor and an acrid taste. It also contains two other alkaloids, *methyl coniine* and *conhydrine*, the former being a colorless liquid and the latter inert and crystallizable.

Conium is incompatible with astringents, vegetable acids, and caustic alkalies.

**PREPARATIONS AND DOSE.**—*Conium* is given in the dose of 3 grains (0.2 Gm.).

*Fluidextractum conii*, N. F. IV (fluid-extract of conium) is produced by maceration and percolation of the drug with diluted alcohol and acetic acid, followed by evaporation. Dose, 3 minims (0.2 c.c.).

**PHYSIOLOGICAL ACTION.**—Upon the gastrointestinal tract conium acts as an irritant, causing nausea and often vomiting and diarrhea. It also causes profuse salivation in larger doses, and sometimes profuse perspiration. It influences both the phrenic and sympathetic nerves, as does curara.

Upon the circulation this drug is depressant, the pulse becoming slow and weak.

Conium at first quickens and deepens the respirations, but later it acts as a depressant, the breathing becoming weak and irregular, and finally ceasing. This action is believed to be exerted through paralysis of the motor nerve-endings in the diaphragm.

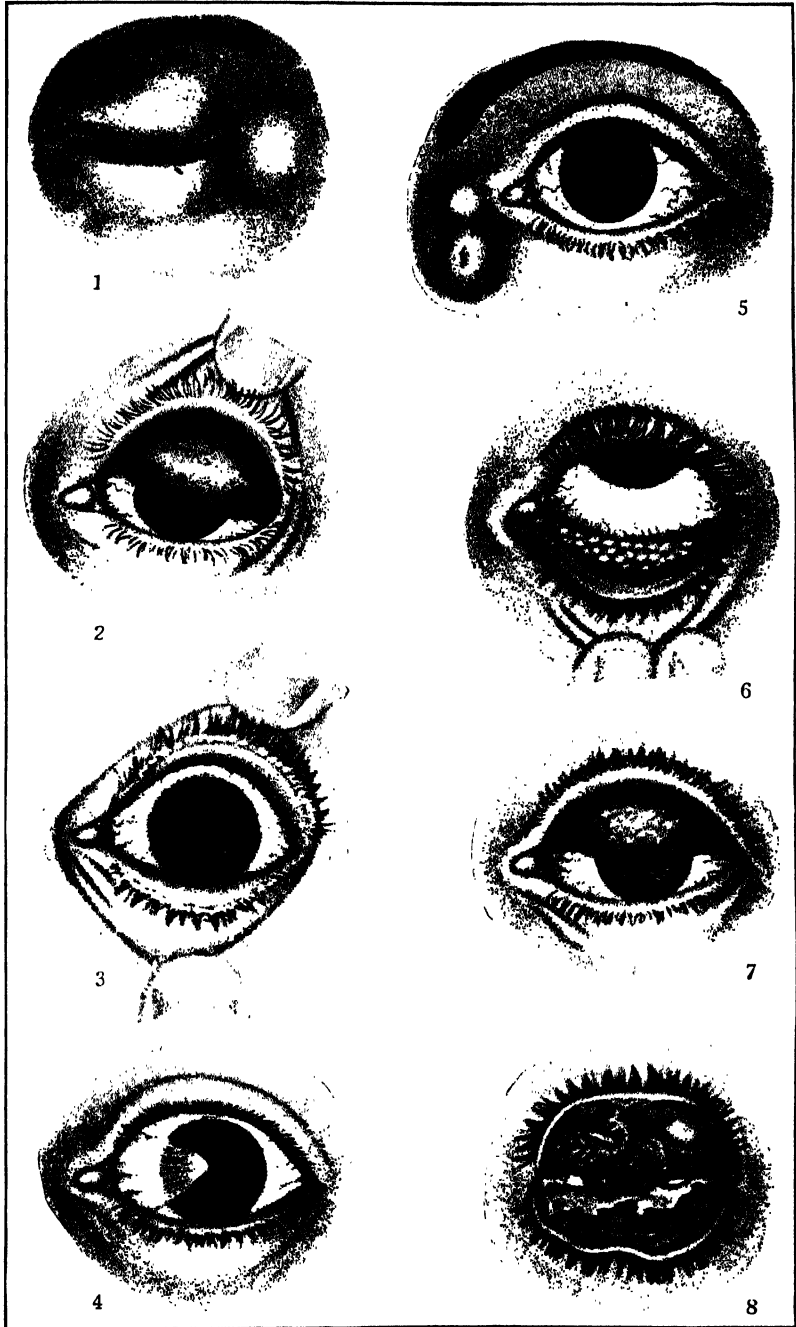
The drug is also depressant to the central nervous system, causing languor and drowsiness, although, even when large doses have been taken, consciousness is usually maintained until just before respiration ceases.

Coniine causes paralysis of the phrenic nerve, and the motor nerves of the accessory muscles of respiration probably become paralyzed later. Very large doses cause general paralysis. Hayashi and Muto (Archiv f. exper. Path. und Pharm., Bd. xlviii, Heft 5 and 6, 1903).

**POISONING BY CONIUM.**—Poisonous doses of this drug cause motor weakness and somnolence, and early there are tremors and twitching. The pupils become dilated and ptosis and staggering occur. This is followed by paralysis, which begins in the lower extremities, the patient gradually losing the power of walking. The condition then extends upward and may reach the tongue, in which case the patient becomes unable to speak, though his intellect remains unimpaired.

**TREATMENT OF CONIUM POISONING.**—The stomach should be evacuated either by the use of emetics or the stomach-pump, and large doses of tannic acid should then be administered. Stimulants, such as strychnine, should be given and external heat applied. Artificial respiration should be instituted as required.

**THERAPEUTICS.**—Owing to the unreliability of its preparations conium is not used extensively. If it is employed at all, the best results will be obtained in spasms due to irritation of nervous structures. It has been used in such spasmodic affections as **epilepsy**, **chorea**, **paralysis agitans**, **pertussis**, **tetanus**, and **acute asthma**. It may relieve the pain in **ulcers** and **cancer** when applied in a poultice, and is a useful depressant in **mania** and **hysteria**. H.



External Diseases of the Eye. (*J. M. Ball.*)

1, suppurative dacryocystitis; 2, trachoma; 3, catarrhal conjunctivitis; 4, pterygium; 5, lachrymal fistula; 6, follicular conjunctivitis; 7, vernal conjunctivitis (tarsal type); 8, tuberculosis of the conjunctiva (*Eyre*).



## CONJUNCTIVA, DISEASES OF THE.

—The conjunctiva is more frequently inflamed than any other ocular tissue; it is not only exposed to invasion by hosts of bacteria, but it offers a favorable nidus for their development. The pathogenic micro-organisms may be carried into its folds in many different ways: through the medium of the hands, towels, handkerchiefs, etc.; through the lachrymal passages, and from the nasal mucous membrane by direct continuity of structure.

The extensive lymphatic and vascular system of the conjunctiva occasions the deposits of organisms there which are more or less laden with toxins and even with microbes themselves, so that the conjunctiva is not infrequently the seat of rheumatic and gonorrheal inflammations and other systemic infections by an endogenous process.

**HYPEREMIA OF THE CONJUNCTIVA.**—Conjunctival hyperemia may either be passive or active. Passive hyperemia exists after paralysis of the cervical sympathetic, or as a result of some interference with the proper circulation of blood in the membrane, or it may be associated with disorders of the general systemic condition, especially gout.

Active hyperemia is a prelude to all inflammatory conditions of the conjunctiva, but may be occasioned by the presence of a foreign body or a misplaced cilia, or by the irritative action of dust and smoke. It is a frequent exponent of some error of refraction or of muscular insufficiency, and is often associated with a catarrhal condition of the nose and throat and with disease of the lachrymal passages.

**SYMPTOMS.**—There is a smarting, burning, and itching sensation in the

eyes, the lids feel heavy, and there is a disinclination to prolonged near and fine work.

On eversion of the eyelids the mucous membrane is found to be abnormally red and perhaps a little swelled, while the Meibomian glands, imbedded in the tarsus, are rendered indistinct by dilated meshes of blood-vessels. The injection of the vascular supply may be limited to the conjunctiva of the lids or involve that of the globe also. There may be a slight increase in the flow of tears, but there is never any discharge.

**TREATMENT.**—Treatment of hyperemia of the conjunctiva resolves itself into the removal of the cause. If of passive origin, the removal of the obstruction to the circulation will be followed by the rapid subsidence in the undue vascularity. If of active, the correction of any existing anomaly of refraction or of muscle balance, or the removal of any foreign body, will accomplish the same result. **Dark glasses** should be given to protect the eyes from irritating rays of light, and from dust and smoke, and a **boric wash** or some other mild antiseptic or astringent lotion will, with **cold compresses**, be sufficient to reduce the vessels to their normal size.

**INFLAMMATION OF THE CONJUNCTIVA.**—When an increased and perverted secretion is added to the symptoms of hyperemia, the conjunctiva may be said to be inflamed.

Many varieties of conjunctivitis are contagious and give rise to a similar form of conjunctivitis when the secretion is inoculated into a healthy eye. It is due to this fact and the virulence with which certain forms of conjunctivitis attack the eye that the large majority of the blind owe their loss of sight to this form of ocular disease.

Bacteriology should be in daily use in every eye clinic: First, because it is an important aid to diagnosis, as the classification of conjunctival inflammation is becoming more and more a bacteriological one. Second, because it is a guide in determining the safety of any operation. Disaster can often be prevented by a thorough bacteriological investigation before attempting to operate. Third, because it materially influences our views of treatment. Prophylaxis is a matter of the first importance. The teachings of modern bacteriology give us important indications as to when an eye should or should not be bandaged. A bandage retains septic secretions, although sometimes it is of use in preventing an ulcer from becoming ectatic. Fergus (Brit. Med. Jour., March 11, 1905).

For the microscopic examination of conjunctival discharge in contagious diseases of the eye the pus should be taken with a platinum loop and spread upon a glass slide. It is important to take the pus from the *cul-de-sac* and not from the edge of the lid, and also to spread the pus very gently.

Rapid staining with Löffler's methylene blue, drying, and examining with a  $\frac{1}{12}$  oil-immersion lens gives the best results. If a deeply stained, encapsulated diplococcus of characteristic shape were seen lying chiefly within the cells, the diagnosis of gonorrheal conjunctivitis was usually warranted. It could only be mistaken for the diplococcus of meningitis. The latter is usually found outside of the cells. Where there is doubt, cultures should be made. The Klebs-Löffler bacillus is rarely found in the secretions from the conjunctiva, and, when a bacillus having its morphological characteristics is observed, culture experiments are required to settle the diagnosis. The Weeks bacillus is by far the commonest organism found in "pink eye," and is readily recognized by slide examination. Edgar S. Thomson (Med. Record, May 17, 1912).

Corneal involvement is a common complication of all forms of conjunctivitis and must always be regarded in the prognosis, as its occurrence usually indicates that there will be a permanent disturbance in vision after the subsidence of the inflammation.

According to the nature of the secretion and the character of the pathological changes observed in the tissues of the conjunctiva, inflammations of that membrane have been divided into the catarrhal, diphtheritic, purulent, granular, phlyctenular, tubercular, and infectious varieties.

### CATARRHAL CONJUNCTIVITIS.

**SYMPTOMS.**—In the simple form the conjunctiva is red, vascular, and swelled, the vessels usually forming a large, coarse network. At first these changes are limited to the palpebral conjunctiva; but they soon extend to the retrotarsal fold, the caruncle, and semilunar folds, and finally to the bulbar conjunctiva. The surface of the membrane is smooth, serving to differentiate it from other forms of conjunctival inflammation. The eyelids are slightly swelled, and their edges reddened and covered with yellowish crusts, and bathed with an abundant secretion.

Severe cases are characterized by the involvement of the bulbar conjunctiva, and by an increase in the redness and swelling of the palpebral portion of the membrane and of the retrotarsal folds. The net-like formation of blood-vessels can no longer be differentiated; small hemorrhages appear, scattered through the membrane, and there is a serous infiltration from both the superficial and deep vessels. This fluid collects in the submucous tissue and occasions chemosis.

The lymph-follicles may develop, and

the papillæ of the conjunctiva become swelled and turgid and give to the membrane a rough and granular appearance.

In chronic forms the objective symptoms are not prominent. There is moderate swelling and congestion of the conjunctiva and but slight secretion, the symptoms being those of hyperemia.

There is a constant sense of heaviness and a sensation of sand in the eyes; there is burning and watering, and vision is momentarily blurred by some of the secretion covering the pupillary area of the cornea.

Epidemic of acute catarrhal conjunctivitis due to the Koch-Weeks bacillus in a rural district embracing about 12,000 inhabitants. Over 200 individuals were affected. The overwhelming majority occurred in children; in all cases both eyes were affected. The cornea was involved in but a single eye in a woman, ending in perfect recovery. Isolation and appropriate treatment soon put a stop to the outbreak. Snell (*Lancet*, Aug. 13, 1904).

Eel serum is known to be toxic by fishermen, fish dealers, and cooks, *i.e.*, locally toxic, but only recently have cases of conjunctivitis from this source been reported. The author has seen 2 such cases. When the blood spurts into the eye of the fish dresser, reddening and smarting result, and eventually a typical conjunctivitis is present. In the laboratory it has long been known that eel serum contains a toxic substance which cannot be isolated, but is inherent in the serum. The latter also exerts a hemolytic action in proportion to its toxicity. It is known that the leech is naturally immune to these activities. Steindorff (*Berl. klin. Woch.*, July 31, 1911).

Given certain conditions under which conjunctivitis appears, a particular location and form of secretion, and rebellious to proper treatment, the possibility of artifacts must be entertained. This holds good

especially in military life. As early as possible a microscopical examination of the secretions should be made in the hope of finding something of diagnostic importance. Often certain kinds of débris may be formed in the lower *cul-de-sac*—cinders, etc. Bacteria should be present, if at all, in atypical fashion, and the usual pathogenics should be readily excluded. The conjunctiva contains normally certain common saprophytes. The cytologic formula in ordinary conjunctivitis contains few or no eosinophiles, but in the artificial forms polynuclear eosinophiles appear to be common. Bollack (*Presse méd.*, Jan. 4, 1917).

**COMPLICATIONS.**—Secondary corneal involvement occurs in the aged, especially when the catarrh has persisted for years. The ulcers are usually at the limbus, and their formation is attended with pain and photophobia. They appear as small, round, gray points, which may become confluent and form a crescentic ulcer. These usually heal, leaving small, bow-shaped nebulæ. Iritis may also present itself, and is usually the result of keratitis; but it may also be seen in severe cases of conjunctivitis without involvement of the cornea.

In gouty persons there is a form of conjunctivitis to which the name of "catarrhorheumatic ophthalmia" has been given, which is attended with great pain in the eyes and temples and great photophobia. There is usually marked lachrymation, but no discharge.

**ETIOLOGY.**—Catarrh of the conjunctiva may be originated by any of the causes of hyperemia of the conjunctiva. It may be the product of foul air or of poorly ventilated rooms, especially when large numbers of people are crowded together, as in tenements, etc.; professions which expose the eyes to overuse or the prolonged action of irri-

tative gases and vapor dispose to it, or it may be set up by contact with a leucorrhœal discharge. It is common in warm and changeable weather, when it may assume an epidemic form.

Koch and Weeks, independently of one another, have isolated a small bacteria, which when inoculated upon the conjunctiva of a rabbit has produced this form of conjunctivitis,—*pink-eye*, *acute epidemic conjunctivitis*. Staphylococci and streptococci may be present.

Study showing that 57.6 per cent. of normal conjunctivæ harbor the xerosis bacillus, 20 per cent. the pneumococcus, 3.8 per cent. the diplobacillus of Morax-Axenfeld, 3.8 per cent. staphylococci, 9.2 per cent. Friedländer's bacillus, 3 per cent. yeast fungi, a few contained unrecognized bacteria, while in only 40 per cent. could no bacteria be found. In the acute cases practically always the conjunctival sac contains the xerosis bacillus immediately after a gonococcal infection, while the pneumococcus, pneumobacillus, and staphylococcus were each present in a few in pure culture. Lynch (N. Y. Med. Jour., March 9, 1912).

Henry S. Gradle, in "Ophthalmology" for July, 1916, has called attention to the swimming pool as a source of conjunctival infection. He quotes Schultz, who, in 1899, reported a series of conjunctival infections traced to swimming pools. Later other German observers recorded a series of cases which resembled trachoma. Brown, of Philadelphia, reported 500 cases that appeared during the summer of 1914. Notwithstanding the daily change of water in swimming tanks, pathological bacteria have been found after the water has been used but a few hours. It is well to note that the salt water swimming tanks are not so dangerous as the fresh water tanks. This is due to the salt in the water, and the chlorine given off by the salt. This does not, however, imply, according to Southard, that frequently changing of the water is not indicated; for bathers can be, and are infected even in salt water pools and tanks. EDITORS.

The course of this variety of conjunctivitis is usually favorable, uncomplicated cases recovering in from one to two weeks. In adults, however, especially if there be a history of alcoholism, albuminuria, or diabetes, the disease may assume a chronic form. Both eyes are usually affected, either at the same time or the second eye a few days later. The disease may begin as an hyperemia and slowly go over into catarrh, or the onset may be more abrupt. In institutions where there are poor hygienic conditions, the disease usually becomes chronic and epidemic.

**TREATMENT.**—Attention should be given to the general health. Any existing systemic disease, such as rheumatism, diabetes, or albuminuria, should be combated; shorter working hours should be prescribed for professional men and more exercise recommended; the eyes must be properly protected from the light, air, and dust with smoked glasses, and they should be kept clean from discharge by frequent washings with **boric acid lotion**; great relief may also be obtained from the application of **ice-compresses**. These are best applied as follows: 1. Several pads of gauze of three or four thicknesses, about the size of a silver dollar, are laid on a block of ice. The ice should be suspended in a receptacle with perforations in its bottom which will permit the water and any secretion from the compress to drain off into a jar beneath it. An ordinary kitchen collander and wash basin will answer very well for this apparatus. One of the pads is taken from the ice as soon as it has been saturated, and is applied to the closed lids, removed in a few moments, and a fresh one substituted for it. 2. Compresses of absorbent cotton which have been

soaked in ice-water may also be employed. They should be squeezed out sufficiently to prevent any of the water trickling over the patient's face and neck. 3. **Cold** may also be applied by means of the ordinary douche or by holding a small cake of ice directly to the eye; but these should be discarded for the compress, as they can only be used intermittently.

To avoid repetition it seems well at this place to give the indications which call for employment of **hot** and **cold compresses** not only in treatment of catarrhal conjunctivitis, but also of the other forms of conjunctivitis as well.

In hyperemia of the conjunctiva, induced by ametropia or the presence of a foreign body, we have, in cold, a simple, but effective means of restoring the membrane to its healthy condition. In these cases the douche or the compress may be applied over the closed lids, with the greatest advantage, for fifteen minutes at a time. The water employed should not be too cold, or excessive reaction may follow its use.

In the severer forms of conjunctivitis, when there is a purulent inflammation or an exudate, ice is the sovereign remedy. When employed in the manner indicated, disastrous results are not to be feared.

At the commencement of the disease the board-like swelling of the disease is, doubtless, one of the chief causes of pyrexia, and, as the swelling and induration prevent the cold from gaining access to the eye, it is necessary that the treatment should be energetic and prolonged. The compresses, therefore, should be maintained night and day in such cases, and should only be desisted from when a corneal ulcer threatens. If this contingency arises, the **ice-compress** should at once be substituted

by the **hot application**, these being persisted in for fifteen minutes every two or three hours. The hot water relieves engorgement of the corneal circulation induced by the intense chemosis of the bulbar conjunctiva and favors resolution of the cornea.

In the treatment of all forms of conjunctivitis **nitrate of silver** occupies a leading position, the strength of the solution employed being proportionate to the intensity of the inflammation and the quantity of the secretion. In the early stages, where the discharge is mucoid in character, it should be employed in the strength of from 2 to 4 grains (0.13 to 0.26 Gm.) to the ounce (30 c.c.) and later, *i.e.*, when the discharge has assumed more of a purulent character, of 10 grains (0.65 Gm.) to the ounce (30 c.c.).

It is always best to apply the silver directly by means of a swab, and when the stronger solutions are employed it should always be neutralized by means of sodium chloride. If corneal ulcer occurs, **atropine** should be at once instilled into the eye. Many discontinue the application of the silver as soon as this complication occurs, but if the discharge be very marked and care be taken to apply the silver in the manner just directed it will usually be found to exercise a most advantageous action upon the course of the disease.

Solutions of **argyrol** may take the place of silver in cases of moderate severity, and may be employed by the patient himself, the former in 30 per cent. strength, the latter in 20 per cent. Both drugs are non-irritating, and should be used at intervals of a few hours, so that their action may be a continuous one, the drugs being made to penetrate into the folds of the conjunc-



tiva, deep in the *culs-de-sac*, and as they gradually exude bring with them the bacteria contained in the secretion.

When the discharge appears, astringents are indicated, but these should not be instilled at night. One-fourth to  $\frac{1}{2}$  grain (0.016 to 0.032 Gm.) of **alum** added to the ounce (30 c.c.) of **zinc solution** is useful, but **silver nitrate** is best. Some of the organic silver preparations may be used in place of it, as **silvol** 10 to 40 per cent., **argyrol** 10 to 30 per cent., **protargol** 10 per cent., or others. These contain a smaller percentage of metallic silver, attack the tissues less, and are much less irritant. They may be entrusted to the patient. Wolfe (Jour. Kans. Med. Soc., Dec., 1917).

## FOLLICULAR CONJUNCTIVITIS.

**DEFINITION.**—Follicular conjunctivitis is a form of catarrhal conjunctivitis attended by a great development of the lymph-follicles.

**SYMPTOMS.**—The inflamed follicles appear as oval, pinkish prominences the size of a pinhead, in the retrotarsal folds, especially the lower. They may be very numerous and may be arranged in parallel rows. In a proportion of the cases they are but few in number, and are scattered over the conjunctiva. There is some photophobia and inability to do near work for any length of time.

**ETIOLOGY.**—Follicular conjunctivitis is frequently seen in epidemic form in schools and asylums, especially where many scholars are massed together, scrofulous subjects being particularly prone to be affected. As there are frequently no subjective symptoms, the physician is often the first to discover the presence of the follicles.

Epidemic of pneumococcic conjunctivitis complicating influenza. Report of 28 personal cases observed during three months, all but 3 in adults.

The prodromes were swelling of the upper lid and swelling and redness of the tarsal conjunctiva. Usually membrane formation followed, often adherent and of a tough consistency, and accompanied by a pronounced follicular hypertrophy. There was moderate purulent secretion, the pneumococci being found both in the secretion and in the membrane. After about ten days' duration a rapid convalescence usually followed. Possek (Wiener klin. Woch., March 11, 1909).

**PATHOLOGY.**—The follicles consist of a mass of round cells, identical with the lymphoid stroma of the conjunctiva. There is no capsule, and the epithelium is unaffected. In the acute form, when the secretion is abundant, the affection is contagious; but, when there is but little discharge, the follicles lie hidden in the *cul-de-sac* without giving rise to any acute symptoms, and contagiousness is not to be feared.

The disease is one of childhood and adolescence, and may be associated with acute or chronic catarrh, but usually with the latter. The follicles disappear totally after a time; so that the prognosis is favorable, notwithstanding the chronicity of the process and its tendency to relapse, which serves to differentiate the disease from trachoma, with which it bears a close resemblance.

**TREATMENT.**—Treatment is the same as for catarrhal conjunctivitis, with the additional indication of bringing about the disappearance of the follicles. This is best accomplished by insufflations of **iodoform**, **aristol**, or **calomel**. In stubborn cases **expression of the follicles** by roller forceps is recommended. The hygienic surroundings should be bettered, if need be, the health of the patient attended to, and all near work prohibited. All errors of refraction should be carefully corrected under **atropine**.

**VERNAL CONJUNCTIVITIS.**

**DEFINITION.**—Vernal conjunctivitis is a chronic catarrhal inflammation of the conjunctiva, usually occurring in children and adolescents, which is attended with the formation of characteristic lesions in the pericorneal and palpebral tissues.

**SYMPTOMS.**—The changes at the margin of the cornea consist in an accumulation of the conjunctival epithelium with hypertrophy of the underlying connective tissue. This gives rise to large, reddish-gray prominences, which may readily be seen. Although located in the palpebral fissure, these may extend for some little distance into the corneal tissue, or surround the entire cornea. The tarsal conjunctiva is thickened in the neighborhood of the diseased area; its papillæ are enlarged and present a characteristic mammillated appearance. When the lids are first everted, the conjunctiva is covered with a fine, bluish-white haze, which resembles a layer of milk. At the height of the process there is profuse lachrymation, but rarely any discharge. An uncontrollable itching and considerable photophobia are complained of.

There is a possibility of mistaking vernal conjunctivitis for trachoma, and the writer describes the following forms of the disease: 1. The eye shows no change, except a slight ciliary injection. The patient has severe photophobia. It is the initial stage of the disease, but is usually of brief duration. The diagnosis is very difficult. 2. In this form, the most typical and also the most common, there is observed degeneration of the tarsal conjunctiva of the upper lid, which presents the appearance of a stone pavement. Conjunctiva of the lower lid is catarrhal, or only hyperemic. This form is often mistaken for trachoma. 3. About the cornea are brownish nodules, which some-

times cross the margin and invade the cornea itself. A network of conjunctival vessels is attached to each nodule. There is more or less photophobia, frequently hyperemia of the iris with ciliary injection, and occasionally hyperemia of the palpebral conjunctiva. This form may be mistaken for phlyctenular keratitis or keratitis fasciculosa. 4. This form is characterized by flat, broad infiltrations of colloidal consistence in the ocular conjunctiva with dense vascular networks attached. It may be confounded with episcleritis. 5. A mixture of the second and third varieties. 6. A mixture of the second and fourth varieties. Although the diagnosis of vernal catarrh is usually easy, a great help in diagnosing the condition is the fact that if the diseased eye is rubbed quickly and gently with the upper lid, or if, after eversion of the lid, the proliferations on the tarsal surface of the conjunctiva are rubbed with a little glass rod, the patient will complain of severe itching. This happens with no other disease. Falta (*Archives of Ophthalmol.*, July, 1905).

The disease usually becomes worse upon the approach of spring, the eyes being comparatively free from irritation in the winter. It is quite rare and generally affects males, being essentially a disease of childhood and adolescence.

Vernal catarrh is more frequent in Turkey than in any other country (about 0.75 per 100 eye patients).

It is much more common in males than in females, in the proportion of 9 to 10. Vernal catarrh is an affection of the warm season; thus, of 92 cases reported, 73 occurred from May to September.

The cases recur from year to year for a number of years, six to eight. Saemisch, who first described the malady, observed a case which recurred for twenty-three years. The disease is almost always bilateral, although the two eyes may be quite differently affected. It is localized in

the tarsal conjunctiva of the upper lid (palpebral form), or at the limbus (pericorneal form), or more frequently in both of these regions at once (mixed form). Complications are very rare; the resistance of the cornea is remarkable and this is one of the points of difference between it and trachoma, which it greatly resembles. The great majority of cases occur between the ages of 10 and 25 years.

The writer further emphasizes a clinical sign consisting of a number of white points developed deeply within the pericorneal swelling. This sign has not been mentioned before, although it occurs in a decided proportion of cases; when present it is a pathognomonic sign of vernal catarrh. Trantas (*Archives d'ophtal.*, Dec., 1905).

The prognosis is good, although the disease runs a very chronic course and may persist from ten to twenty years. It finally disappears, however, leaving no trace, except in rare cases, in which a faint haze may remain on the cornea.

**ETIOLOGY.**—The disease frequently occurs in gouty subjects, but the primary cause is unknown.

The writer found that the conjunctival secretion in vernal catarrh is rich in eosinophile polymorphonuclear leucocytes. This has been confirmed by several other observers. In the spring of 1910 2 cases of typical vernal catarrh came under his care showing this peculiarity, and he was led by them to examine smears stained with Giemsa taken from all the cases of conjunctivitis seen by him. These included all the ordinary forms and, in those of conjunctivitis of known cause, eosinophile cells were very rare, but, in a number of those of unknown cause and no bacterial finding, he found abundance of them; 13 cases occurred in the writer's small clinic, 10 of which were first diagnosed by the abundance of eosinophile cells. When

it is considered that vernal catarrh is usually thought to be a rare disease the importance of this observation is evident. Brown Pusey (*Jour. Amer. Med. Assoc.*, April 1, 1911).

The excised pieces showed intense hyperemia of the blood-vessels and a colossal dilatation of the lymphatics. The cell infiltration of the substance proper was in all cases very marked and consisted, in accordance with the extant investigations of others, of plasma, eosinophiles, mast-cells, lymphocytes, and fibroblasts. A formation of follicles was nowhere observed. The plica abounded in elastic fibers.

The excised pieces of the ocular conjunctiva exhibited infiltration with plasma-cells, chiefly around the vessels. In the above-mentioned thickened parts the epithelium all over sent conform and tubular processes into the depth, between which the connective tissue was sclerosed; the substance proper contained very dense cellular infiltrations, exclusively of eosinophile and plasma-cells. There were no traces of elastic fibers.

Thus, the final proof seems established that in vernal conjunctivitis every portion of the conjunctiva may occasionally be invaded by the inflammatory process. R. Seefelder (*Klin. Mon. f. Aug.*, Dec., 1911).

**TREATMENT.**—The disease is incurable, and palliation of the acute symptoms represents all that can be done. Van Milligen, who has had excellent opportunities to study the disease in Constantinople, has employed a solution of **acetic acid**, 1 to 20 grains (0.06 to 1.3 Gm.) to the ounce (30 c.c.), with marked benefit.

As there is no discharge, the disease is not really a catarrh, and does not demand the same treatment as this class of cases. The eyes should be kept clean with a 10-grain-to-the-ounce (0.65 Gm. to 30 c.c.) solution of **boric acid**; **dark glasses** should be prescribed to

protect the eyes from the light and other irritants, such as dust, smoke, etc. If there is much pericorneal injection, **atropine** in small doses should be prescribed. **Massage** of the lids with a 1 per cent. salve of **yellow oxide of mercury** seems to exercise a favorable effect. **Iced compresses** diminish the vascularity and afford marked relief. **Arsenic, quinine, and iron** should be administered internally.

Extirpation of the hypertrophied papillæ by **electrolysis**, and **obliteration** of the **superficial vessels** supplying the growth in the limbus, have been resorted to with good results.

### **PURULENT CONJUNCTIVITIS.**

**DEFINITION.**—Purulent conjunctivitis is an acute, contagious inflammation of the conjunctiva caused by infection with gonorrheal virus, and attended by a copious, purulent discharge. It is one of the most dangerous and virulent diseases of the eye. The contagion is carried by micro-organisms, the gonococci of Neisser, which appear not only in the pus, but also in the superficial layers of the conjunctiva itself. The gonococci may be found in isolated groups, either in the pus-cells or epithelial cells, and their virulence depends upon the severity of the urethral disease at the time of infection; the more violent the latter, the greater the ocular inflammation.

Purulent conjunctivitis may be produced during any stage of the urethral disease, but about the third week of the existence of the latter is the most dangerous period, the discharge being then very copious, thick, and noxious. The discharge from a gleet may, however, give rise to severe and even destructive gonorrheal ophthalmia.

According as the affection occurs in

adults or infants, it is called *gonorrheal ophthalmia* or *ophthalmia neonatorum*.

### **GONORRHEAL OPHTHALMIA.**

**DEFINITION.**—Purulent or gonorrheal ophthalmia is a specific purulent inflammation of the conjunctiva characterized by great swelling of the lids and conjunctiva, and by copious secretion of contagious pus, presenting a marked tendency to destruction of the cornea.

**SYMPTOMS.**—The period of incubation varies, according to the intensity of the contagion, from a few hours to five days.

From a few hours up to 6 days after infection the conjunctiva begins to show a yellowish, blood-stained secretion which soon changes to a greenish yellow. The cornea may begin to ulcerate in 24 hours. The prognosis is graver in adults, probably from the mixed infection; 95 per cent. of the new-born recover under proper treatment while 45 per cent. of the adults affected lose vision in that eye, even with specialist care. The main point is prophylaxis. It is more difficult in men as their hands get contaminated at each micturition, but towels, handkerchiefs, bath water, etc., may convey the contagion, as also animals. Children with vaginitis should wear closed drawers. Washing the hands, after relieving any calls of nature, should be enforced for young and old. E. F. Montano (*Gaceta de la Acad. de Méd., Mexico, Jan.-June, 1917*).

At first the signs of a simple catarrhal conjunctivitis may alone be present, but soon the lids become red and so tumefied and tense that the patient is no longer able to open them. The palpebral conjunctiva and retrotarsal folds also become intensely red and swelled, and the former is often speckled with hemorrhages. The membrane

becomes hard and granular, owing to an infiltration of seroplastic lymph into its substance. The bulbar conjunctiva soon becomes similarly swelled, forming a hard rim about the cornea. The discharge is at first watery and sanious, but soon changes to a yellow or greenish-yellow pus. The eye is painful to the touch, and there is intense pain in the eye and temple. The constitutional symptoms are often severe, the patients being generally in a weak and feeble condition. Slight fever is also present in some cases.

This stage—that of infiltration—lasts about three days, when the disease attains its height. The lids then become less tense, the conjunctiva softer, and a copious purulent secretion follows. After a week the discharge gradually declines, the tissues undergo restoration, and, at the end of four to six weeks, beyond a condition of chronic inflammation of the conjunctiva, which persists many weeks, the parts resume their normal appearance. Cicatrices rarely follow.

At times the disease assumes more of a subacute type. All the signs of inflammation are then less severe, the palpebral conjunctiva being alone affected, and it is often only possible to diagnose these cases from catarrh of the conjunctiva by a microscopical examination. When the disease is particularly virulent, it may simulate the croupous type, a false membrane being formed, which gives the conjunctiva a yellowish-gray appearance.

**COMPLICATIONS.**—The chief danger in purulent conjunctivitis is the implication of the cornea. It results from the pressure of the swelled tissues; the corrosive action of the secretion, including the invasion of the gonococci, and direct continuity of in-

flammation to the substance of the cornea.

At first the cornea may look dull and slightly clouded; but soon circumscribed areas of grayish infiltration appear, which soon become more dense and yellow, and then form ulcers. The ulceration usually occurs at the limbus, and may lead to rapid perforation. In many instances, this is a relatively favorable result, as further infiltration of the cornea is frequently prevented thereby. In other cases, however, the infiltration may form at the margin of the cornea and extend a considerable distance around its circumference, giving rise to a marginal ring ulcer. Sloughing of a great portion or even the whole of the cornea usually follows, and the eye is usually lost.

The ulceration may also occur at the center of the cornea, when the whole cornea becomes opaque. As a rule, the greater the severity of the conjunctivitis, the greater the liability to corneal involvement, especially if the bulbar conjunctiva be much chemosed. As a rule, also, the earlier the corneal ulcers form, the more likely are they to result seriously.

Corneal ulceration usually appears on about the third day, but this depends upon the severity of the inflammation; in a certain number of cases it does not appear until late in the disease.

Iritis may supervene when the ulceration has extended to the deeper layers of the cornea or when perforation has occurred. It generally gives rise to great ciliary neuralgia, photophobia, and lachrymation.

The inflammation may extend from the iris to the other ocular tissues, and a panophthalmitis be set up.

Prognosis depends entirely upon the degree of implication of the bulbar con-

junctiva, for, if this be much chemosed, corneal ulceration will probably occur and vision be seriously compromised.

**ETIOLOGY.**—Gonorrheal ophthalmia arises through infection with gonorrheal pus alone, the virus being conveyed directly from the genitalia to the eyes, or from a diseased eye of another person, or from the patient's fellow-eye by the hand, handkerchief, etc.

Sequelæ are the result of corneal involvement, for the conjunctiva is usually restored to a healthy condition; but, in the event of the corneal ulceration, all eventualities are possible; from a slight degree of opacity, on the one hand, to adherent leucoma, panophthalmitis, or even atrophy of the globe, on the other.

**TREATMENT.**—The chief indication in the treatment consists in carefully and frequently freeing the eyes of the copious secretion; for this purpose **bichloride of mercury** or **boric acid** solutions should be employed every hour or even every half-hour. To do this properly will require the constant care of two intelligent attendants. The patient should be put to bed, and, if but one eye be affected, its fellow should be carefully protected. For this purpose the device of Buller answers admirably. This consists in a watch-glass held in place before the eye by strips of adhesive plaster. It should be removed every forty-eight hours and the eye thoroughly cleansed with a solution of boric acid. The surgeon should warn the patient of the danger of carrying any of the urethral discharge to the eyes and should caution the nurses about exercising the most punctilious cleanliness as regards their hands, and care in the use of towels, handkerchiefs, etc.

• Great care should always be exercised

in washing the eyes of these cases, as the pus frequently spurts out like a jet when the lids are separated.

If the swelling of the lids prevents ready access to the *cul-de-sac*, **canthoplasty** should be performed, as this procedure not only gives access to the *culs-de-sac*, but lessens the pressure of the lids, and gives room for the infection to spread.

In the first stage, **ice-compresses** should be applied constantly night and day and changed every few moments. In robust subjects or when there is intense initial pain or swelling, marked relief may often be obtained by **leeching** the temples.

In the second stage, when the conjunctiva has become velvety and the discharge purulent, the conjunctiva should be touched daily with **silver nitrate** (15 to 20 grains—1 to 1.3 Gm.—to the ounce—30 c.c.—of water), to reduce the swelling and the amount of secretion. The silver nitrate solution should be applied by the surgeon to the conjunctiva of the everted lids and then neutralized with a saturated **solution of common salt**, as directed in catarrhal conjunctivitis. The eye should also be kept bathed in a 30 per cent. freshly prepared solution of **argyrol**.

In purulent ophthalmia the policy of treatment should be guided by four considerations: the careful, thorough use of proper antiseptics, efficient but not too irritating; watchful care over corneal and general nutrition; free drainage, and especially avoidance of even the slightest injuries to the delicate corneal epithelium. A bacteriological examination of the discharge should be made as soon as possible, and, while the author uses generally a 1 per cent. **nitrate of silver** solution in virulent gonorrheal infections, a 2 per cent. or even stronger solution for a few treatments

may be better. In certain mild non-gonorrheal infections 0.5 per cent. is usually sufficient. M. D. Stevenson (Jour. Amer. Med. Assoc., July 8, 1911).

According to the writer, he has found **cresatine** (metacresol-acetic acid-ester) a synthetic phenol derivative, a specific in gonorrheal ophthalmia. One application of the pure cresatine on a cotton swab to the cocaineized cornea and conjunctiva usually gives marked and speedy relief of symptoms and the disappearance of the gonococci. A second application is sometimes necessary, but a third rarely so. A 25 per cent. solution in liquid petrolatum is an efficient prophylactic. This treatment limits the duration of the ophthalmia to 24 or 48 hours after the first application. Cresatine is absolutely non-injurious to the tissue cells of the cornea or conjunctiva. Barnett (Med. Rec., Feb. 5, 1916).

It is best to delay the application of silver so long as the conjunctiva is hard and infiltrated and the discharge is watery. A croupous membrane also contraindicates its use.

In the third stage, when the signs of chronic conjunctivitis appear, the silver should be substituted by crystals of **zinc** and **copper**, but these should only be employed when the cornea is quite free from all signs of acute inflammation and ulceration. During the entire course of the disease, the cornea should be carefully inspected, and, at the first appearance of ulceration, **atropine** should be instilled. This drug frequently serves a double purpose in combating any existing iritis, as well as the corneal involvement. If corneal ulceration be present, great care must be exercised in making the applications of **silver** to the everted lids, as pressure on the globe might cause rupture of the ulcer. Care should also be exercised

to prevent the silver coming in contact with the infiltrated cornea.

Fifteen severe cases treated by local application of **steam**, to kill gonococci. As soon as the eyelids can be everted—iced compresses having been applied—the conjunctival sac is syringed with **potassium permanganate** solution, dried with gauze, and treated with **steam**, the neighboring skin being protected with linen or wet gauze. Where chemosis is marked, the ocular conjunctiva is also steamed, care being taken to avoid the cornea. Ten patients with corneas uninvolved rapidly and completely recovered, the discharge ceasing early; in the other 5 cases the conjunctivitis was cured, together with, in one instance, the cornea. The steam treatment is considered superior to silver nitrate. Goldzieher (Wiener klin. Woch.; Lancet, March 2, 1912).

The present methods of treating this disease are in great measure to blame for the poor results obtained in adults. The writers suggest the following as the result of extensive trial: The patient must be confined to bed at once and kept there until the danger has passed. The **diet** is to be very light and to consist largely of milk. The bowels are to be kept open; **aspirin** and **quinine** are to be given. The local treatment is by far the most important and consists in a constant, unintermitting irrigation of the eye with warm **potassium permanganate** solution of the strength of 1:15,000 to 1:20,000 in the early stages. Later **boric acid** in about 2 per cent. solution can be substituted. There must be no manipulation of the lids, as this is the cause of much harm, through trauma too small to be seen, but none the less dangerous. The duration of the irrigation must be about eight days, with absolutely no interruption. At the end of this time minor local measures may be resorted to if the conditions call for any further treatment. Hosford and James (Lancet, Jan. 13, 1912).

## OPHTHALMIA NEONATORUM.

**DEFINITION.**—This is a purulent inflammation of the conjunctiva occurring in the newborn, characterized by great swelling of the lids and conjunctiva, and the copious discharge of contagious pus.

This is one of the most frequent of eye diseases, and is responsible for more cases of blindness than any other affection, the statistics showing that from 30 to 60 per cent. of the inmates of the different blind-asylums throughout the country owe their infirmity to its ravages. Of the 300,000 blind in Europe, 30,000 were rendered so by ophthalmia neonatorum.

**SYMPTOMS.**—The disease usually appears on the second or third, more rarely on the fourth or fifth, day after birth. In the latter case, however, it is probable that infection is carried to the eyes after birth, either from the mother or the nurse or some other person suffering from gonorrhea.

The active symptoms are the same as in gonorrheal conjunctivitis, except that they are not so severe. The swelling of the lids is not so great, and the secretion is less copious. The bulbar chemosis does not attain such a high degree, and corneal complications are not so frequent nor so serious.

The disease may occur in a severe type, with a tendency to invade the cornea; or it may run a milder course, without corneal complication.

The prognosis depends upon the state of the cornea when the case comes under treatment. If this be uninvolved, the chances of recovery are favorable.

**ETIOLOGY.**—The origin of the contagion is the morbid vaginal secretion, the infection, as a rule, occurring at the time of birth by some of the secre-

tion of the vagina being transferred to the lids of the infant and being carried into the eye the first time that the child's eyes are opened.

The writer was able to infect monkeys with the secretions from ophthalmia neonatorum, free from gonococci, but containing cell inclusions such as Prowazek has described as trachoma bodies. The course of the transmitted affection resembled in every respect that of transmitted trachoma. Lindner (Wiener klin. Woch., Nov. 11, 1909).

Ophthalmia neonatorum not the work of the gonococcus is generally of the inclusion type, and silver nitrate prophylaxis has no influence on it. Sometimes this type accompanies the ordinary type of ophthalmia neonatorum. The inclusion ophthalmia may persist for weeks up to two months in spite of the most approved and systematic measures of treatment and leave a thickening of the conjunctival *culs-de-sac* in the form of a series of parallel folds seen when the lower lid is everted, but there seems to be no danger of ulceration of the cornea. The writer found the inclusions in 15 out of 20 cases of ophthalmia neonatorum and Lindner found them in 53 pure and in 4 cases mixed in 110 cases of ophthalmia. Morax (Annales de gynéc. et d'obstet., June, 1911).

**PROPHYLAXIS.**—The great aim should be the prevention of contagion during birth. If this be done there is no disease in which prophylactic measures are so efficacious and the results obtained so gratifying. Since the adoption by ophthalmologists of adequate measures, the proportion of cases of ophthalmia neonatorum has been reduced from 7.5 per cent. to 0.5 per cent. Vaginal antiseptics should be employed before labor. Immediately the child is born, the lids should be wiped with a piece of lint saturated in **bichloride solution (1:8000)**.



Of 388 newly born infants admitted to the wards of the Massachusetts Charitable Eye and Ear Infirmary in a period of four years, 23 were discharged from the hospital totally blind and 42 partially so, all so disabled that their future livelihood is made seriously more difficult. The vision of 67 was affected at the time of their appearance at the hospital. Of this series of cases, 272 were attended at birth by physicians in private practice, 30 by dispensary physicians, 63 by physicians in hospitals, 13 by doctors employed by the city, 10 by midwives, 3 were unattended, and in 5 cases the attendant could not be determined. Of the 65 babies who became blind or partially so, 55 cases occurred in private practice; 4 cases, or about 6.3 per cent., of all attended by hospital physicians, and 3 cases, or 33.3 per cent., of those attended by midwives. Mackenzie (Boston Med. and Surg. Jour., May 16, 1912).

After the child has been washed, during which care should be taken that none of the water is permitted to gain access to the conjunctival sac, a drop of a 2 per cent. solution of **silver nitrate** should be dropped into each eye. The solution of silver in this strength excites considerable irritation, and, while its application should always be insisted upon in hospitals and the like, in private practice, where no gonorrheal contagion is suspected, the douche before labor and the cleansing of the lids by **bichloride solution**, followed by a careful douching of the conjunctival *cul-de-sac* with **boric acid**; will suffice.

In making the applications the child should be laid on its back and its head placed between the knees of the physician, while an assistant seated in front should hold its body in his lap and secure the hands. The lids should then be gently separated by pulling on the skin of the eyelids above the upper and

below the lower tarsus, and complete eversion of both lids performed.

The writer treated one eye with 2 per cent. **silver nitrate** and the other eye with 1 per cent. **silver acetate** in 50 infants in his practice and found that the results were fully as good with the acetate as with the nitrate. The acetate has the advantage that it is harmless under all circumstances, which cannot be said of the silver nitrate. Seefelder (Munch. med. Woch., Bd. liv, Nu. 10, 1907)

1. Immediately following the birth of the infant the eyes should be carefully wiped with sterile gauze dipped in a saturated solution of **boric acid**, and then a 5 per cent. **sophol**, 25 to 50 per cent. **argyrol**, or 10 to 20 per cent. **protargol** solution used as a prophylactic against ophthalmia neonatorum.

Late infection comprises one-fourth of the cases of ophthalmia neonatorum, and may be due to faulty application of the prophylactic, or latent gonorrhea. More often it is the result of contamination from the vaginal secretion because of lack of vigilance, or ignorance on the part of attendant or mother; therefore, the nurse should be instructed to thoroughly scrub her hands with soap and water and disinfect them before washing the infant's eyes, dressing the navel, and bathing the mother. The mother's hands should be cleansed several times daily, particular attention being given to the nails, and she should be repeatedly warned as to the danger of the lochia. By careful attention to these precautions the morbidity from ophthalmia can be greatly reduced, if not entirely controlled.

2. The solutions should be dispensed in amber-colored sterile tubes sealed with paraffin for use by midwives; a small quantity of sterile gauze should be placed in the prophylactic package.

3. Suitable instructions as to technique should be printed on the birth certificate.

4. Legislation should be enacted for the control of midwives.

5. Midwives should be compelled to make report of births within twenty-four hours following delivery.

6. The health department should furnish the drugs gratuitously to indigent cases.

7. In cases of ophthalmia occurring in patients under the charge of midwives they should be required to summon a physician immediately or notify the health department promptly. Committee Report (Amer. Jour. of Obstet., Feb., 1910).

If a solution of **silver nitrate** stronger than 2 per cent. is used, there is a possibility of setting up a so-called "silver catarrh." Because of evaporation, old solutions are often found of greater strength than is expected.

The writer prefers **silver acetate**, for at 14° C. (57.2° F.) it is only soluble to the amount of 1.02 per cent. Its action is as prompt as that of silver nitrate, and, according to some authors, is even better. Hans Treber (Wien. klin. Rundsch., Nu. 35, 1911).

The writer recalls the great value of prophylaxis in regard to infection of the eyes following childbirth. In order to determine the best solution for use by the midwives, one that would not cause damage if carelessly used, he experimented on the web of frogs' feet with solutions of silver nitrate, silver acetate, argentin, protargol, and silver acetate, followed by salt solution and "sophol." Of these the **silver acetate** is recommended, as not more than a 1 per cent. solution can be made at ordinary temperatures. It also does not become concentrated at the usual temperature and can be preserved indefinitely. In experimenting with silver nitrate it was found that as a result of evaporation the solution increased in the course of five months from a 1 per cent. to an 8 per cent. concentration. In an open bottle it increased from 1 to 3 per cent. in 2 days. Zweifel (Zentralbl. f. Gynäk., July 6, 1912).

**TREATMENT.**—The treatment is the same as has just been given under the gonorrheal ophthalmia of adults, with the exception that the protection of the sound eye and the application of compresses are not, as a rule, feasible.

**GRANULAR CONJUNCTIVITIS (TRACHOMA, EGYPTIAN OPTHALMIA, MILIARY OPTHALMIA).**

**DEFINITION.**—Granular conjunctivitis is an inflammation of the conjunctiva, characterized by the hypertrophy of the tissues and by the development of small, pinkish prominences or granulations on the conjunctiva, the chief tendency of which is to undergo absorption and produce serious cicatricial changes in the lids.

Although it was generally supposed that the disease was introduced into Europe from Egypt by Napoleon's army in 1798, it was subsequently shown that the disease had actually been endemic in Europe centuries before. Excellent descriptions of the disease were recorded by the ancients, and measures adopted by them for its relief have come to light again in our own day under the form of the operation of scarification. Nevertheless, to Napoleon is due, in large measure, the propagation of the disease, for it was doubtless owed to the frequency with which his armies came in contact with those of other countries, as well as with the civil population, that the disease spread so rapidly during the first part of the last century.

The Jews, the Irish, the inhabitants of the East, and the North American Indians are especially liable to the affection, while negroes are practically exempt.

Geographically, the disease occurs more often in Arabia and Egypt, while western Europe is more exempt than

eastern Europe. In the United States it affects those dwelling in tenement houses, and is associated with unhygienic surroundings in large cities. It is found scattered widely over the country, though high altitudes seem to render a certain immunity to the disease.

**SYMPTOMS.**—There is a great difference in the symptoms not only on account of the intensity of the changes, but also from the rapidity of the course of the disease. The signs of irritation are greater, the quicker the course of the disease. Usually, the irritation symptoms are only moderate, but slight photophobia, lachrymation, and pain being complained of.

Not seldom the disease is so insidious that the subject does not know of its existence, the disturbance in vision due to corneal complication giving the first indication. At other times the disease begins with marked inflammatory symptoms; the lids are edematous, the conjunctiva swollen, and there is a rich secretion of pus.

Granular conjunctivitis may occur in either an acute or chronic form, according as it is or is not attended by the signs of acute inflammation.

**Acute Granular Conjunctivitis** (*Papillary Trachoma; Chronic Blepharorrhoea*).—This is rare in this country, and should be differentiated from the violent exacerbations to which the chronic forms of the malady are liable. In this variety there are all the signs of purulent conjunctivitis, with the development of the granulations. The lids swell, and the conjunctiva, both bulbar and palpebral, becomes injected. The papillæ are enlarged, and the characteristic granulations are about the size of the head of a pin, and are situated, for the most part, in the retrotarsal folds—chiefly the upper. They are also found

scattered throughout the conjunctival membrane.

At first, lachrymation is usually marked, but, later, considerable discharge appears, and superficial ulcers form at the limbus.

After several weeks the disease gradually subsides, usually leaving some cicatrices in the lids to indicate its presence, although in other cases, after the absorption of the granulations, the mucous membrane may be quite smooth.

If the inflammation be but slight and not sufficient to absorb the granulations, the process may run into the chronic form.

The disease which the United States Government recognizes as trachoma, and which is contagious, is described as follows: A characteristic connective-tissue hyperplasia occurs in the eyelid; as the lymphoid cells proliferate, the follicles tend to degenerate and to become encapsulated by the newly formed connective tissue. In connection with this process new blood-vessels are also formed, which permeate to some extent the interior of the follicle. As the inflammatory process continues, these little round, firm capsules are pushed up into the conjunctiva. Their contents break down. The overlying conjunctiva becomes involved in the same degeneration and gives way. The contents of the capsule are discharged and the little spot of destroyed conjunctiva is replaced by scar-tissue. In this way the disease tends to destroy bit by bit the entire conjunctiva. Safford (*Med. Record*, Nov. 11, 1911).

Trachoma, although a disease confined to the superficial tissues in and overlying the orbit, is as little known and as intractable as it was a century ago. Halberstaedter and Prowaczek attribute the disease to infection by the germ *chlamydozoön*. As to the pathology of the disease it appears that in the protoplasm of the epithelial cells of the infected conjunc-

tiva granules first appear, as large as ordinary cocci, or larger, which, as they multiply, become separated, so that they inclose a cavity devoid of granules. In this cavity very minute granules appear later, which are smaller than cocci and which stain differently from the granules that are developed first. The seat of infection is in the upper folds, the rigid tarsal cartilage protecting the germs in their destructive work. Stewart (St. Paul Med. Jour., May, 1912).

Examination of 4000 children of Porto Rican schools, showed 9.5 per cent. suffering from trachoma, and classed 5.4 per cent. more as "suspicious." Exclusion from the schools or segregation of all trachomatous pupils is favored. King (Public Health Reports, Dec. 18, 1914).

The Annual Report of the Surgeon General of the United States Public Health Service states that the best solution of the trachoma problem has been found to be the establishment of small hospitals for the treatment of the disease in localities in which it is prevalent; and that the service, therefore, now maintains five trachoma hospitals in the three States of Kentucky, Virginia, and West Virginia. In the past fiscal year 12,000 cases of the disease were treated, and in addition the hospitals have been used as centers for educational work. In Kentucky, of 18,016 people examined, 7 per cent. were found to be suffering from trachoma. (Med. Rec., Mar. 18, 1916).

**Chronic granular conjunctivitis** is usually primary, but it may be due at times to the imperfect disappearance of the acute granulations. The constant factor in this variety of trachoma is the trachoma-follicle, as it exists in the different degrees in which these conditions are met with.

The development of chronic granular conjunctivitis is often very insidious. Usually, at first, marked lachrymation is present, although there is but little

secretion. If the cornea has become vascular, photophobia may be a most distressing symptom. The lids are swelled, and, upon their eversion, the characteristic granulations spring into view. They resemble sago-like prominences arranged in parallel rows, and are found in the superficial layers of the conjunctiva, especially in the fornix. Rarely a few smaller isolated granules will be seen on the bulbar conjunctiva. At first they are found in the lower *cul-de-sac*, but the upper *cul-de-sac* is soon affected showing a great development of follicles.

After a few weeks or months the granulations give rise to a more or less active vascular reaction, attended with swelling of the papillæ and a mucopurulent discharge. The papillæ may become so large that they may obscure the granulations. Occasionally the granulations become absorbed, but in the majority of cases fresh eruptions of follicles present themselves during the period of regressive inflammation and go through the same changes as their predecessors.

After a certain duration, grayish lines of fibrous tissue make their appearance, and the final stage of cicatrization begins. As a result of this, dense scar-tissue forms; this exerts traction upon the tarsus—already softened by the pre-existing disease—and produces the deformities of the lids so characteristic of the affection.

**COMPLICATIONS.**—The corneal complication may take the form of pannus or of ulceration.

**Pannus** consists in the formation of a vascular tissue of new formation on the cornea, which begins at the limbus and invades the center. At the location of the pannus the surface of the cornea is uneven and roughened, and there is a superficial gray and

transparent haze, which is infiltrated by numerous vessels; these originate from the blood-vessels of the conjunctiva. The pannus usually begins in the upper part of the cornea and frequently stops below, in a sharp, straight, horizontal border line. Later, it may develop at other parts of the limbus; so that the entire cornea may become covered. Vision is affected as soon as the pannus reaches the pupil, which, if the cornea be entirely covered, may be reduced to light-perception.

When ulceration occurs, it is either at the edge of the pannus or upon a portion of the cornea which had hitherto been uninvolved. It usually occasions great photophobia and lachrymation.

The hypertrophy of the conjunctiva increases until the diseased process has run its course, when it begins to shrink, and is replaced by cicatricial tissue, with all its attendant evil consequences to the normal contour and function of the lids. The degree of cicatrization depends upon the severity of the early stages of the disease.

The beginning of the scar formation shows itself in the tarsal conjunctiva, narrow, whitish lines permeating the latter. These lines become more numerous and form a fine network, which gradually spreads; the conjunctiva included within the meshes becomes attenuated, until quite smooth and white.

The hypertrophied conjunctiva in the fornix gradually shrinks, becoming shorter, and the folds of the conjunctiva in that location disappear. This is known as *symblepharon posterior*. In extreme cases the *culs-de-sac* are reduced to shallow fissures between the lid and the globe. The lids become distorted, through the cicatricial changes in the cornea and tarsus, the latter participating in the inflammation, as well as

the conjunctiva. It becomes much hypertrophied, especially along its lower margin, where the conjunctival vessels perforate it. It is especially in this position that the shrinking of the conjunctiva, which follows later, makes itself most felt, and is the main factor in the production of the bow-like distortion of the lids, produced by trachoma. The cilia no longer occupy their normal position, but become displaced, and cause great irritation by being brought in contact with the cornea. This irritation is further augmented if the shrinkage of the tarsus continues, and entropion is produced.

**Ectropion**, of the lower lid especially, may also be originated, owing to the contraction of the orbicularis exerted upon the lids—already prone to eversion by the swelling of the conjunctiva.

**Xerosis** of the conjunctiva occurs as a result of the cicatrices. The blood-supply to the conjunctiva is shut off and its epithelium undergoes fatty degeneration. The surface of the membrane then becomes dry and smooth and almost leathery, and the corneal epithelium also becomes thicker and its transparency much interfered with. The eye finally becomes blind and a source of continued annoyance, by reason of the constant sensation of local dryness experienced.

The pannus may clear up entirely, leaving a normal cornea beneath. If there be ulceration, however, opacities remain, which disturb vision according to the extent to which they involve the pupillary area of the cornea. Frequently, as a result of pannus, there occurs a connective-tissue metamorphosis, which greatly interferes with the transparency of the cornea. Another result of pannus sometimes is a bulging,

or staphylomatous, condition of the cornea, the tissues of which have become so altered that they give way before the normal intraocular tension.

**ETIOLOGY.**—In general, the disease may be said to arise from poor hygienic conditions. It develops in institutions where the inmates are crowded together, in armies, orphan-asylums, almshouses, and the like. It is probable that the so-called lymphatic or scrofulous temperament predisposes toward it, although the disease may attack those in perfect health.

The disease is primarily a disease of poverty, congestion, and poor hygienic surroundings. Even in places where and among people in whom the disease is endemic, the better classes are almost entirely exempt. The disease is said to have had its origin in Asia and Africa, and to have been introduced into Europe, from Egypt, by Napoleon's soldiers; hence its name of Egyptian ophthalmia. Trachoma is especially prevalent along the Mediterranean coasts of Europe, Africa, and Asia, being very common among the Egyptians, Arabs, Armenians, and Syrians. In southern Europe, among the Poles and Hungarians, as well as among the Polish and Russian Jews, it is fairly common. In France it is rare. The Germans and the Russians are not commonly affected by it, but along the German-Russian border it is common. In northern Europe, with the exception of a few imported cases, it is not common. H. M. Friedman (N. Y. Med. Jour., Sept. 21, 1912).

Trachoma always arises through infection from another eye already infected, by means of the secretion; only under exceptional circumstances, when the air is heavily charged with the poison, can it be the medium of communication of the disease. The infectious nature of the secretion is doubt-

less due to micro-organisms; but, while numerous bacteria are found in the secretion, gonococci, streptococci, etc., the specific germ has not yet been isolated.

As the secretion alone causes the infection, therefore, the danger of infection depends upon the strength of the secretion; the richer this is, the greater will the danger be to surrounding persons.

Chlamydozoa—an alleged cause of trachoma—were found in the discharges of patients with so-called "swimming tank conjunctivitis." In most cases the clinical picture was one of acute trachoma, and there was a history of the use of the public tanks very shortly before the lesions appeared. Huntemüller and Paderstein (Deut. med. Woch., Jan. 9-16, 1913).

The transfer of secretion from one eye to another is usually accomplished by the fingers or toilet articles which are brought into contact with the eyes, as handkerchiefs, towels, sponges, etc. This is more apt to happen when numbers are crowded together and are likely to use these articles in common.

Trachoma is on the increase in Cuba, as shown by the following figures, taken from J. Santoz Fernandez's clinic, which registers 3000 new patients each year: From 1875 to 1902 there were 2.25 per cent. of cases of trachoma; from 1903 to 1907 the percentage rose to 4.91 per cent.; in 1908 it was 5.88 per cent.; in 1909 almost 8 per cent., and in 1910 there were 10 per cent. F. M. Fernandez (Med. Record, June 17, 1911).

Unknown in Belgium before the campaign in Egypt, military ophthalmia, as trachoma was then called, attacked the army with a frightful severity. In 1834 all the soldiers having trachoma were sent home and in this way the disease was spread to the rural districts. However, trachoma is rare in the provinces of the south and the east, although in the

north and west it is very frequent, up to 20 per cent. of the population frequenting the polyclinics being affected. Brandes (*Soc. Médico-chir. d'Anvers*, Dec. 2, 1911).

In Knott, Perry, Leslie, Breathitt, Lee, Owsley, and Clark Counties, Kentucky, a total of 3974 people were examined, and 500 of these, or 12½ per cent., were found to be suffering from trachoma in its various stages. The diagnosis of trachoma, for the purpose of this report, was made only in positive cases; those only suspicious were not included, but doubtless some of them were beginning trachoma. Corneal complications, pannus, etc., were very frequent.

Of the total number examined, 2796 were school-children from the mountain counties; 338, or about 12 per cent., had undoubted trachoma, while in Clark County, which is in the blue-grass region, where living conditions are totally different, only 15 cases, or about 3 per cent., were found affected among the 436 school-children examined. A total of 3232 school-children were examined.

If conditions as found in the child are to be taken as an index of what is in the home, certainly a 12 per cent. average of trachoma among the school-children indicates an appalling amount of trachoma in the homes of these good and honest people in the mountains.

Dr. Stucky reports that in one mountain county he examined 100 cases in two days, 25 per cent. of whom had trachoma or some infectious disease of the eyes. Also in another mountain county he examined over 200 cases; 25 per cent. and more of these had trachoma. "Many of them," he writes, "were the most pitiful and hopeless I had even seen."

It is obvious that trachoma is plentiful, but it is difficult, outside of schools and public institutions, to secure the examination of sufficient numbers to give exact percentages. However, on the opening day of court week in a county seat the

writer examined the eyes of 245 people in a routine manner, regardless of whether any diseased condition existed, and found that 45 of them, or about 18 per cent., had trachoma and about 10 per cent. showed corneal complications. The majority of these were men, heads of families, attending court from all sections of that county. John McMullen (*Public Health Reports*, Nov. 8, 1912).

**PATHOLOGY.**—In trachoma we see an excessive degree of development of the papillæ of the mucous membrane and the formation of the granulations. Microscopically, the granulations may have an imperfect capsule or may have no capsule, but they seem to grow from, or in, the stroma of the conjunctiva. In the acute form the granulations consist of lymph-cells alone. They are to be regarded as new growths in the conjunctiva, and, in addition to the lymphoid cells, the mass of cells and connective tissue is penetrated by blood-vessels. The chronic granulations consist of lymph-cells toward the surface, but their bases are formed chiefly of connective tissue. Gradually the cellular elements are transformed into connective tissue, and in this way cicatricial degeneration of the conjunctiva is brought about at each spot where a granulation was seated.

The development of the papillæ is not characteristic of trachoma, for it is present in moderate degree in every lasting inflammation of the conjunctiva, as in chronic catarrh, vernal and follicular catarrh, and purulent conjunctivitis.

**PROGNOSIS.**—Acute granular conjunctivitis, or trachoma, is characterized by its chronicity and by the serious consequences to vision; this, added to its contagiousness, makes it one of the most dreaded of eye diseases. Relapses occur frequently and persistently and may

occasion all of the intense inflammatory symptoms of acute granulations. Its great danger lies in its contagiousness and the great rapidity with which it spreads through schools or any institutions where large numbers of inmates are gathered together, by the careless use of towels and common utensils. The prognosis is, therefore, always grave, and demands the adoption of great precautions to prevent a disastrous epidemic.

**TREATMENT.**—Prophylaxis is obviously of the greatest importance, and, as the conspicuously dangerous element is the secretion, cleanliness, adequate air-space, and proper ventilation of the sleeping-rooms must be insisted upon in all crowded institutions. Every patient should be provided with his own basin and towel, or, better still, should be required to wash under "running water." When the disease is once established, rigorous isolation of all those afflicted should be practised.

The chief aim of the treatment must be to check the development of the hypertrophy of the conjunctiva, and bring about absorption of the granulations in order to prevent the destruction of the mucous membrane, and to reduce the previous results of the disease to a minimum.

In the early stages, frequent washings of the conjunctiva with a 10-grain solution (0.6 Gm.) of **boric acid** and **bichloride solutions** should be employed; especially is this true of acute granulations. If there be much pain and photophobia and some haze of the cornea, **atropine** should be instilled in conjunction with the cleansing lotions. A **nitrate of silver** solution should be employed so soon as the discharge becomes marked, in the same manner and to meet the same in-

dications as already described in the treatment of other forms of conjunctivitis.

The usual routine treatment of trachoma by copper sulphate, tannic glyceride, argyrol, etc., has shown but poor results when applied to the thousands of school children on the records of the Health Department of New York. The intense **bichloride rub**, however, combined with the treatment indicated to modify the intense reaction which often follows the first few applications, is so far superior to the other methods that it should supersede them in nearly all cases. It leaves no scar tissue. Beals (N. Y. Med. Jour., Nov. 13, 1915).

The treatment of chronic granular conjunctivitis in the early stages must be non-irritating; but, so soon as the discharge becomes marked, **silver nitrate** becomes the sovereign remedy. When the acute stage has moderated and the discharge is less marked, the silver salt should be replaced by other caustics: **copper, alum, zinc**, etc. These drugs must be continued months and perhaps even years, until every trace of hypertrophy has gone and the conjunctiva has become perfectly smooth and clean.

The **nitrate of silver** solution should be applied but once daily, and, at times when there are marked signs of irritation, must be wholly withdrawn for a few days, while these are combated with **atropine** and milder antiseptics.

After trying everything he could think of the writer found that a 1 per cent. solution of **silver nitrate** daily, and a 10 per cent. solution of **argyrol** 3 times a day or more were beneficial. The silver nitrate seemed most effective when dropped directly into the conjunctival sac, for forcible closure of the lids spreads the caustic into the depths of the transitional folds, the parts most affected. H. S. Gradle (Ophthalmology, July, 1916).



As it is necessary that the local treatment shall be continued for such a long time during the stage of cicatrization, to prevent relapses, an ointment of 1 grain (0.06 Gm.) of **tannin** to 1 dram (4 Gm.) of **vaselin** may be ordered and may be applied by the patient himself. **Copper** may be applied in the same strength.

The writer recommends a 10 per cent. solution of **copper sulphate** in glycerin, put in the patient's hands with instructions to dilute 1 drop in 20 drops of water and to use freely on the eye from four to six times as the best home treatment for chronic trachoma. A. E. Prince (Jour. Amer. Med. Assoc., April 25, 1908).

Numerous **surgical procedures** have been proposed for the excision of the granulations, and some observers advise the excision of the entire fornix of the conjunctiva. It is probable, however, that the resultant cicatrices cause more mischief than those which would result if the disease were allowed to take its course. This form of treatment has, therefore, met with but little favor from the more conservative clinicians.

A good, free **canthoplasty** is the first step in treatment, the vesicles being then destroyed by **electrolysis** or scrubbed well with antiseptics. In some cases **excision** of the **conjunctival folds** is advisable. If rolling or crushing is thoroughly done, too much healthy tissue is macerated and broken down. Stewart (St. Paul Med. Jour., May, 1912).

The results of surgical removal of the **tarsal cartilage** and **palpebral conjunctiva** in 402 cases of trachoma are given by the writers. They contend that the efficiency of this operation seems to be known to but few. In most of their cases where recovery occurred, vision had been reduced to counting fingers. D. W. White and P. C. White (Ophthalmology, Oct., 1915).

A less harmful method, and one which is frequently employed by the ophthalmologists of this country, at least, consists in the **expression** of the **granulations** by means of forceps. Knapp has devised a roller forceps especially for this purpose.

The surgical treatment of trachoma is the most effective way of combating the disease. **Expression** is safe and effective, shortening the duration of treatment in a marked degree. The operation can be performed under **cocaine**, but in severe cases and in intractable children **ether** and **gas** are preferable. Adhesions in the lids should be separated with the probe daily until the tissues of the lids have healed. The reaction caused by the operation yields readily to **iced cloths** applied to the lids, and the resulting traumatic conjunctivitis can be controlled in a few days with a **silver salt**. The after-treatment is most important to attain complete cure and to prevent recurrence, and should continue some weeks. W. M. Carhart (Amer. Jour. of Surg., June, 1908).

After an experience in 15,000 cases, the writer recommends the following procedure, which, with unimportant variations, is the method used among the oculists in Egypt: The upper lid is turned and seized between the thumb and index finger, between which it is squeezed as hard as possible. The object of this is to bring out all the follicles that are hiding in the tarsus, which is completely relaxed by this procedure. The upper lid is then given another turn so as to bring into view the fornix, and all follicles, granulations, or papillary hypertrophies are carefully **scarified**. The same is repeated on the lower lid. Every trachomatous point is then gone over with a sharp curette until the characteristic scraping of the tarsus is felt, especial attention being paid to the fornices. After well irrigating the sac, **yellow oxide** ointment is applied, and a moist bandage used for two hours. After

that the eyes are washed every two hours.

On the following six to eight days the lids are touched with a 2 per cent. solution of **silver nitrate** until entire cessation of the secretion. Then he changes to 1 to 2 per cent. **glycerite of copper sulphate**. Thus in fifteen to twenty days, sometimes in ten, complete cicatrization is attained, thus shortening the usual time of treatment greatly. In 8 to 10 per cent. of the cases there occurred relapses or rather reinfections; in these cases the same method was again used successfully. Alexandria Jacobides (La Clinique ophtalmol.; Hahnemannian Monthly, March, 1912).

The results of treatment of trachoma with **iodic acid** obtained in the Military Hospital in Krakau, where this method of treatment has replaced all others since 1906, are given by the writer. The iodic acid is moistened until it forms a plastic mass which is rolled into a rod. For comparison 583 cases thus treated were compared with 553 cases treated by other methods. The average length of treatment was 44.12 days in the former, and 64.47 in the latter. Ulcer and pannus occurred in 0.85 per cent. of the former, in 3.25 per cent. of the latter. Disturbances of vision were 0.51 per cent. in the former, 3.07 per cent. in the latter. Relapses occurred more rarely after treatment with iodic acid, with a difference of 8 per cent. The eye is **cocainized**, the iodic acid rod is applied to the lower transition fold, which is then wiped dry with cotton and the superfluous iodic acid washed off with 3 per cent. **boric acid solution**. The upper lid is then everted and an application made in the same manner; the lid is then doubly everted with a forceps, and the upper transition fold cauterized in the same way. After cauterization the follicles should appear yellow. Pain begins as soon as the effect of the cocaine wears off and varies in severity. A violent inflammation ensues, but after this passes off, the conjunctiva pre-

sents a clean wound surface. Symblepharon must be guarded against. Josef Rudas (N. Y. Med. Jour., from Arch. of Ophthal., Sept., 1913).

The reaction following this procedure is at times quite severe; so that it is advisable to employ **ice-compresses** for some time afterward; to prevent a recurrence of the granulations it is always well to follow the expression by applications of **silver nitrate**.

The writer tried a method of treatment which yielded excellent results, and was recommended to him by La Torro, of Vera Cruz, Mexico. The granulations disappeared in a short time and the conjunctiva was left smooth and clean. The method is as follows:—

With a cotton swab immersed in a 10 per cent. solution of **cocaine** the conjunctiva of both lids is bathed to produce anesthesia. One minute later another cotton swab well soaked with distilled water is impregnated with powdered **sodium salicylate** and rubbed with some degree of strength against the granulations in front and behind the *cul-de-sac*. The lids are, of course, very well everted. In some cases the drug causes some burning; in others this is intense, but in all cases the burning sensation disappears in a short time. For two or three days the conjunctiva becomes gradually smoothed, the granulations disappear by absorption and destruction, the friction used destroying many and increasing a slight inflammation caused by the salicylate. The treatment is repeated every three or four days. More than half of the cases received five or six applications. Of nearly 400 cases thus treated failure occurred in less than 10 cases. F. M. Fernandez (Med. Record, June 17, 1911).

The treatment of trachoma with **carbon dioxide snow** was found more rapid in action and less annoying to the patient than other measures. The applications are made after local

analgesia by a 3 per cent. solution of cocaine. At each sitting 5 or 6 applications can be made to different points on the everted upper lid, and 3 or 4 to the lower lid, spaces being left between the several points. Galetti (N. Y. Med. Jour., from *Revue de therap. médico-chir.*, Jan. 15, 1914).

**Radium** has been tried with success by Cohn, of Breslau, and others.

A large number of cases of trachoma of all varieties have been treated by the writer with radium, and with good results. The exposures were made for fifteen minutes every second day, so that the total exposure was from 150 to 200 minutes. The results at first were not satisfactory, in that the papillary vegetations, the follicular granulations, and the pannus were not macroscopically changed. It was found, however, that only a very brief treatment with **copper sulphate** was necessary to bring about a complete cure after radium had been employed. Fortunati (*Klin.-therap. Woch.*, June 7, 1909).

The writer advocates **tarsal massage**, particularly the improved technique of Vessius and Kuhnt. The writer employs a metal or glass rod about 8 inches in length and about  $\frac{1}{4}$  inch in diameter. One end of it is smoothly rolled with cotton for about 2 inches and moistened in a normal salt, boric acid or boroglyceride solution, or better, one of 1:5000 bichloride. This is used to thoroughly flood the conjunctival folds, dilating the pupil and completely cocaineizing the conjunctiva. The lid is then turned over. The cotton-tipped end of the rod is inserted under the tarsus and deep into the retrotarsal folds; pressure is made upward and the lid is rolled. The thumb that holds the lid over is pressed down upon it, producing undulations in the tarsus. The contents of the follicles are now pressed out, making the tarsus pliable. Great care must be used against injuring

the cornea. The rolling is performed every other day. Dimitry (N. O. Med. and Surg. Jour., Dec., 1915).

The greatest emphasis must be laid upon the necessity of placing the subjects under the best hygienic conditions. In the case of patients confined to hospitals, asylums, etc., the utmost pains should be taken to secure **good ventilation, nourishing food, and perfect cleanliness**, personal as well as general.

When pannus has occurred and the thickening of the conjunctiva subsides, the corneal disease will usually abate *pari passu*; so that the treatment of pannus and of ulcers of the cornea resolves itself into that of the conjunctiva. **Atropine** should be instilled to combat any existing iritis.

If the pannus is unusually dense and is partly made up of connective tissue, further absorption may be obtained by exciting a violent inflammation of the conjunctiva. An infusion of **jequirity** is frequently employed for this purpose. This is prepared by steeping the ground jequirity bean for twenty-four hours in cold water. With this infusion, the conjunctiva of the everted lids is painted thoroughly two or three times daily. A croupopurulent conjunctivitis is excited and is combated in the same manner as already described under this disease. When the inflammation has run its course, the cornea is frequently found to have regained, in a measure, its former transparency.

**Jequirity** is a useful drug in pannus due to trachoma. The writer commences with a very weak solution (0.25 per cent.) at first and uses a fresh solution every day. A. E. Prince (*Jour. Amer. Med. Assoc.*, April 25, 1908).

The operation of **peritomy**, which consists in the destruction of the vessels supplying the pannus, has also been

much vaunted for the cure of this condition. After a ring of conjunctival tissue about 5 mm. from the margin of the cornea is excised by scissors, the underlying connective tissue is dissected off the sclera, which is then laid bare.

Xerosis admits of palliation only by emollients—such as **glycerin**, **olive oil**, or **vaselin**—applied freely several times daily.

The distortion of the lids, with the resultant trichiasis and entropion and ectropion which it occasions, only yields to operative measures.

### **PHLYCTENULAR CONJUNCTIVITIS (LYMPHATIC, OR STRUMOUS, CONJUNCTIVITIS; CONJUNCTIVITIS ECZEMATOSA).**

**DEFINITION.**—Phlyctenular conjunctivitis is a frequent form of inflammation of the conjunctiva characterized by the eruption of one or more grayish elevations or phlyctenulæ on the bulbar conjunctiva. It usually occurs in scrofulous children under 10 years of age.

**SYMPTOMS.**—Children suffering from this disease have the characteristic strumous appearance. They are either pale and thin or bloated and flabby. The cervical lymphatics are enlarged and the nose and upper lip tumefied. There is a moist, eczematous eruption on the face and constant watering of the eyes and nose. Otorrhea is frequent. A distressing symptom—intense fear of light and blepharospasm, due to the corneal involvement, which occurs in most cases of phlyctenular conjunctivitis—completes a clinical picture which renders an examination of the eyes almost superfluous.

An inspection of the eye, however, will reveal the presence of phlyctenulæ. These appear as minute, red eminences,

either alone or in numbers. In the latter case they are situated on the limbus of the conjunctiva and resemble grains of fine sand.

In the simple, or solitary, variety the injection of the blood-vessels is localized immediately around each phlyctenula; but in the multiple, or miliary, variety the conjunctival injection is general and is usually quite marked. In the latter variety there is also much photophobia and lachrymation and rarely some discharge. Usually there is an eruption of these phlyctenulæ on the cornea as well. This is always accompanied by an increase in the photophobia and lachrymation and adds greatly to the gravity of the disease.

**ETIOLOGY.**—Phlyctenular conjunctivitis occurs chiefly among the poorer classes, and is fostered by the improper and insufficient nourishment which they receive and by their damp and unhygienic surroundings. It may be found, however, in children, otherwise healthy, whose vitality has been depressed by febrile disturbances, such as measles, whooping-cough, scarlet fever, and the like. The disease rarely occurs in adults, and only when a tendency toward this disease was manifested in youth. Evidence is accumulating to the effect that it is due to or connected with tuberculosis in a large proportion of cases.

Study of 50 cases of conjunctivitis eczematosa, including results of von Pirquet tests; the local, focal, and constitutional effects of the test; therapeutic administration of **tuberculin**; the local, focal, and constitutional effects of the therapeutic injection, and results of the therapeutic injection on the ocular disease. In addition to the therapeutic use of tuberculin, the patients were given the usual local ocular treatment of conjunctivitis eczematosa (**boric solu-**

tion, yellow oxide of mercury, calomel, atropine, warm compresses, etc.) as indicated, and constitutional measures, such as regulation of diet, hygienic conditions, systematic life, exercise, fresh air, tonics, etc., and where complications, such as hypertrophied tonsils, nasal obstructions, adenoids, or other diseased conditions, existed, these were corrected or treated. The writer concludes as follows: 1. The tuberculous nature of conjunctivitis eczematosa is established, and this opinion is supported by the results obtained in the cases subjected to tuberculin, both diagnostically and therapeutically, and by the majority of the other essential clinical findings. R. J. Tivnen (Jour. Amer. Med. Assoc., Dec. 9, 1911).

The nodular cellular lymphoid deposits, or phlyctenules, of the corneoscleral border may be eye manifestations of a systemic dyscrasia, suggesting in majority of cases some form of tuberculosis. While the microscopical sections of these nodules show giant cells, it does not follow that the nodules are tubercular, but rather indicate that the cellular infiltrate is a manifestation of the disease and not the cause. In 37 cases 7 were found with pulmonary tuberculosis; 16 had some form of tuberculosis; 32 had a positive von Pirquet; 18 had adenoids and diseased tonsils; 6 showed the tubercle bacillus in sections; 4 showed tubercle bacilli in the sputum; 8 physical examinations suggested some form of lung involvement; 15 had a positive Wassermann reaction, 11 negative; 7 had some member of the family with tuberculosis. L. J. Goldbach (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., July 7, 1917).

A clinical study of 92 cases of phlyctenular conjunctivitis revealed the presence of tuberculosis in 90 cases, as shown by a positive von Pirquet test. In the 2 giving a negative reaction, the diagnosis was doubtful. No other condition, either local or general, could be found with

sufficient frequency even to suggest any direct influence in producing the disease. Phlyctenules were produced experimentally in tuberculous rabbits in eight instances; 6 times as a complication of a conjunctival reaction resulting from the instillation of tuberculin, twice in the absence of local irritation of any kind. Numerous attempts to produce the condition in animals not tuberculous were unsuccessful. The pathology of the experimental lesions was similar to that of human phlyctenules. The microscopic findings suggested a tuberculous origin. W. S. Gibson (Amer. Jour. Dis. of Children, Feb., 1918).

**PATHOLOGY.**—A phlyctenula consists of an accumulation of lymphoid cells packed closely together around a nerve-filament, just beneath the epithelium of the conjunctiva or cornea. Soon after its formation the apex of the mass begins to undergo softening and liquefaction. The epithelial covering is thrown off and a shallow ulcer remains. The softening process continues, the epithelium dips down into the ulcer, and healing occurs in ten to fourteen days.

After a time, however, a fresh outbreak of these small, grayish nodules occurs; so that the disease may extend over months and at times years, until the age of puberty is attained, when the eye seems to become protected against further attacks.

In consequence of the corneal involvement, which is usually associated with phlyctenular conjunctivitis, there is always a greater or less degree of cloudiness of that membrane; so that vision is interfered with and the patient rendered incapable of fine work. The scars left upon the cornea are often unsightly.

**TREATMENT.**—This must be directed, in the first place, toward the improvement of the general condition. Notwithstanding the photophobia,

**open-air exercise** should be positively enjoined, as it is absolutely essential for the well-being of the child. All bandages should be removed, the eyes being protected by **tinted glasses** or a generous shade. The skin should be rendered more active by **cold** or **salt baths**, followed by **brisk rubbing**. The nourishment should be strengthening and administered at regular intervals. No feeding should be permitted between meals; all sweets and pastry should be prohibited, while milk, fresh eggs, red meat (once daily), and proper fruits should represent the bulk of the **diet** recommended.

Internally, **calomel** is of value to improve the state of the mucous membrane of the alimentary tract; **codliver oil**, **syrup of the iodide of iron**, **syrup of the phosphate of lime**, and **arsenic** may also be administered with advantage.

The treatment based on tuberculosis as cause, is hygienic, with **tuberculin** injections—bouillon filtrate—in doses varying from 0.000001 to 15 milligrams. Prolonged tuberculin injections with small doses are important, the pulse, respiration, and temperature being watched carefully. L. J. Goldbach (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., July 7, 1917).

It is remarkable that **gray powder**, or small doses of **calomel**, should prove so beneficial, and its success in improving the general condition of these children bears out the opinion that gastro-intestinal autointoxication holds an important place in the etiology. The exhibition of these drugs seems to be especially satisfactory in the fat, apparently over-nourished cases that are met with. The ill-nourished demand the usual building up with **cod-liver oil**, combined with the **phosphate** or **iodide of iron**; but even in these the mercurial drugs are

very valuable. The diet is summed up in little **starchy food**, and more **meat**, **vegetables** and **fruit**. Cridland (Birmingham Med. Rev., May, 1918).

Locally, any existing blepharitis or eczematous eruption about the eye should be combated with **white precipitate ointment** (1 to 2 per cent.) and with **silver nitrate**, after the removal of crusts with **soda solution**.

In the simple form, where there is but little irritation, **calomel** should be dusted into the eyes once daily. This drug combines with the tears, and forms a weak solution of **bichloride of mercury**, which exerts a most beneficial action upon the conjunctiva. Care, however, must be observed that iodine is not being administered internally at the same time with the calomel, for the latter in this event forms with the iodine an iodide of mercury which is very irritating.

A salve of the **yellow oxide of mercury** may be substituted for the calomel often with great advantage.

In the miliary variety, or when there is recent corneal involvement with signs of active irritation, these drugs, which are irritating, should not be applied. In these cases the eyes should be kept clean with frequent washings with **boric acid**, and **atropine** should be instilled at regular intervals.

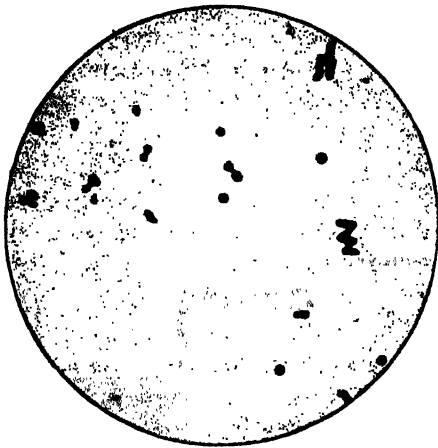
The photophobia and blepharospasm usually subside with the improvement in the conjunctival condition. Should it be very distressing, however, much relief may be had by **cold baths** or from **immersions of the child's head** in a basin of **cold water**.

### CROUPOUS CONJUNCTIVITIS.

**DEFINITION.**—Croupous conjunctivitis is a catarrhal inflammation of the conjunctiva in which there occurs for-

mation of a plastic exudate upon the conjunctival surfaces.

**SYMPTOMS.**—It usually begins with the symptoms of an acute catarrh, but soon attains a severity not witnessed in ordinary catarrh. The lids become edematous, the conjunctiva much reddened and swelled, especially in the fornix, and a discharge, at first seropurulent, but later mucopurulent, appears. The tarsal mucous membrane and retro-tarsal folds become covered with a gray-



Pathology of chronic membranous conjunctivitis. (Howe.)

ish-white membrane, the bulbar conjunctiva being but rarely involved. The pseudomembrane can be stripped off, disclosing a raw and perhaps bleeding mucous surface beneath, which serves to distinguish it from the diphtheritic variety.

The pseudomembrane usually disappears after two weeks; the conjunctiva and lids reassume their normal appearance, and the signs of an ordinary catarrhal conjunctivitis reappear. There are no resultant cicatrices and vision is but seldom affected, the cornea being only involved when the false membrane spreads to the bulbar conjunctiva, which is of rare occurrence.

**DIAGNOSIS.**—The main affections from which croupous conjunctivitis are to be differentiated are diphtheritic conjunctivitis and ophthalmia neonatorum.

**Diphtheritic Conjunctivitis.**—Instead of being limited to the surface of the conjunctiva, the membrane in diphtheritic conjunctivitis involves its deeper layers. The lids are hard and the bulbar conjunctiva is involved, and there is frequent corneal ulceration.

**Ophthalmia Neonatorum.**—In this disease, purulent conjunctivitis, the discharge is much more copious and purulent. Pseudomembranous conjunctivitis is never found among the newborn.

**PATHOLOGY.**—The local inflammation must be regarded as a severe form of catarrh only, in which, owing to the intensity of the inflammatory process, the secretion is richer in fibrin and more prone to coagulation. Various grades of this plastic quality appear. In light cases it may manifest itself as a simple condensation of the secretion, flakes of fibrin forming, which can be readily washed off the conjunctiva. In some cases, however, the exudate has the tenacity of a true diphtheritic membrane. The eye may, however, be the seat of primary infection and true diphtheria occur. Diphtheritic conjunctivitis may also occur as a complication of the general disease.

Case of chronic membranous conjunctivitis. A boy, 8 years old, had been under observation for eighteen months, with a thick, firmly attached, yellowish-white membrane covering the conjunctiva of the upper lid. Treatment had exerted but little influence upon the membrane, although it was then becoming thinner. The eyeball had not been seriously damaged. But at one time in its course there had been a severe exacerbation of the disease in the eye, with soreness of the throat and patches of

similar membrane on the tonsils, and rise of temperature. Two children that he came in contact with in the same ward at this time developed diphtheria and died. A sister of this boy had presented a similar chronic membranous conjunctivitis. After it had lasted nearly a year and a half she developed scarlatina with diphtheritic patches in the throat. This was accompanied by aggravation of the eye symptoms, and necrosis of the cornea, with loss of useful vision in both eyes.

Although both these cases were carefully studied bacteriologically, and many micro-organisms discovered, the Klebs-Loeffler bacillus was present in each case only during the exacerbation, and not at any other time. (See illustration.) Lucien Howe (Trans. Amer. Ophth. Soc., 1897).

Fatal case of diphtheria of the conjunctiva in an infant 11 months old which was wasted and had evidently been neglected. A bacteriological examination showed the Klebs-Löffler bacillus. Diphtheria of the conjunctiva is far from rare in London. Of 3412 eye patients seen at two hospitals for children there were 43 instances of the disease. Nearly two-thirds of the cases were met with in children under 3 years of age. The cases were most frequent during the period when ordinary diphtheria was rife. Three only of the entire number belong to the severe types of the disease. A significant fact in the case described is that the patient died from a toxemia due to conjunctival diphtheria alone, as no membrane could be found in the nose, mouth, or fauces. Most of the fatal cases so far reported have had involvement of the nose, throat, and eyes. S. Stephenson (Ophthalmoscope, Aug., 1904).

Two cases of diphtheritic conjunctivitis, one of them fatal. This complication is more frequent than is generally supposed. The fatal case was secondary to tonsillar infection and was first seen in an advanced stage of the disease. The other seemed to be a primary infection, and

the patient recovered with the administration of two doses of 4000 units each of antitoxin. The diagnosis is easy with the microscope, and the treatment is that of other diphtheritic infections—the use of antitoxin. The importance of early attention to all cases of “running ears,” “sore eyes,” and “discharging noses,” especially in school-children, as possible causes of diphtheria epidemics, is emphasized by the author. M. Bertola (Jour. Amer. Med. Assoc., Jan. 16, 1909).

Cases of diphtheritic conjunctivitis in which the eye was probably the primary seat of infection, as the nasal and pharyngeal symptoms came on several days after the appearance of the conjunctival disorder. Smears from the membranous rhinitis and pharyngitis showed diphtheritic bacilli identical with those from the eye coexisted. The eye inflammation, while resembling that due to the Koch-Weeks bacillus or to pneumococci, differed clinically, especially at first, in the absence of mucous or purulent secretion, in the resistance to ordinary treatment, and in the appearance of minute spots along the intermarginal border. Later mixed infection occurred, as is not uncommon. The age of the patient, 56, is exceptional. H. Friedenwald (Jour. Amer. Med. Assoc., May 20, 1911).

**ETIOLOGY.**—Croupous conjunctivitis is a disease of childhood, and usually develops at first dentition. Its causal factors are the same as those of catarrh, but certain pyrexias, particularly measles and pseudomembranous vulvitis, predispose to it. It may be associated with croup of the larynx, trachea, and bronchial tubes.

**TREATMENT.**—Hot-water compresses should be applied night and day until the pseudomembrane is removed. The general health should be seen to, and purgatives administered to produce watery evacuations.



All caustics and irritants should be avoided so long as the pseudomembrane is present, but the eye should frequently be washed with **bichlorate of mercury** (1:5000), **boric acid**, **chlorate of potash**, or **chloride of sodium** lotions. As soon as the stage of acute catarrh sets in, the treatment should be the same as in acute conjunctivitis.

### DIPHTherITIC CONJUNCTIVITIS.

**DEFINITION.**—Diphtheritic conjunctivitis is an infrequent specific inflammation of the conjunctiva, attended by the formation of a plastic exudate within the layers of the bulbar and tarsal membrane.

**SYMPTOMS.**—The exudation penetrates deeply into the tissue and causes its death, thereby destroying the nutrition of the cornea and causing subsequent loss of that membrane. The lids become hard, board-like, and tumefied. At first there is a scanty seropurulent or sanious discharge, which is followed by a more purulent one as the disease progresses. The secretion is very contagious, and, if there be abrasions at the orifices of the mouth and nose, the membrane will quickly invade them. Patches of membrane are often found in the pharynx and nares.

After the period of infiltration—which lasts from one to two weeks—has subsided, the membrane is thrown off, leaving a raw, granulated surface. At times the membrane may be absorbed. After a time vascularization sets in and the symptoms of an ordinary purulent conjunctivitis supervene. The termination of the process, however, is less favorable than in the catarrhal form, for during the period of cicatrization changes occur which cause atrophy and shrinking of the conjunc-

tiva, and not infrequently occasions great deformation of the lids.

**COMPLICATIONS.**—The chief complication is corneal involvement, which occurs in the vast majority of the cases, and occasions the intense pain by which the disease is accompanied. As a rule, the cornea is affected early in the affection, either by ulceration or diffuse infiltration.

**ETIOLOGY.**—The disease is of specific origin, and the constant presence of Löffler's bacillus has led to the assumption of this germ being the causal factor in the diphtheritic process.

Children between the ages of 2 and 8 years are usually affected, both eyes being involved. The disease is rare in this country, but is not infrequent abroad, where it occurs in an epidemic form. The prognosis is decidedly grave on account of the tendency toward corneal involvement.

**TREATMENT.**—In the first stage, when the lids are hard and board-like, and there is a necessity of limiting the amount of exudation, **ice-compresses** should be employed, but **hot compresses** are indicated as soon as the cornea shows signs of involvement. Treatment must be tentative. Mild antiseptic lotions should be employed to remove all secretions, either **bichloride of mercury** (1:8000) or **potassium permanganate** in 2 per cent. solution. **Silver nitrate** is contraindicated in the early stages, but may be utilized when the membrane comes away. **Atropine** should be instilled early on account of the tendency to corneal involvement. Great attention should be directed toward building up the general health. **Mercury** and **quinine** should be administered and stimulants ordered if the child shows signs of collapse. The

**isolation** of the patients is necessary to prevent further contagion. **Antitoxin**, both subcutaneously and locally, has been used advantageously.

Treatment by **antitoxin** of 25 cases of diphtheritic conjunctivitis occurring among 8000 cases of diphtheria at the Boston City Hospital. In all these cases the Klebs-Löffler bacillus was present in the discharge from the nose. Eight cases were admitted for ocular diphtheria; the others were faucial diphtheria which had incidentally a membrane on the conjunctiva. All were treated with antitoxin, the first dose being 4000 units. Usually a second dose of like amount was given at the end of six or eight hours, and some had three or four injections. Such cases in twenty-four hours usually were doing well, and after forty-eight hours no more anxiety was felt for the eyes. In those cases in which there were corneal ulceration the antitoxin favorably influenced the corneal lesion, and with the exception of 4 cases the patients left the hospital with good vision. In 1 of these 4 cases the cornea upon admission seemed to be wholly necrotic. Six months later there was considerable vision. An opaque scar occupied approximately half the cornea. In the 3 other cases every cornea was lost. These 3 patients had diphtheritic infection during an attack of measles. This probably accounted for the severity of the corneal process. M. Standish (Boston Med. and Surg. Jour., Oct. 2, 1902).

Antitoxin injected beneath the conjunctiva of rabbits has no marked local reaction. It does not seem to neutralize the local condition due to the toxin of the infection if the dose is insufficient to immunize the whole body of the animal. Hypodermic injections of antitoxin is the only effectual method of treating conjunctival diphtheria. Instillations and subconjunctival injections of antitoxin seem futile. For local treatment irritants should not be employed, either as irrigations or as

applications. We should use either sterile water or mild solutions of boric acid, sodium hyposulphite, or potassium permanganate (1:3000). Friction, massage, etc., should not be employed to remove the false membrane.

In the prevention of corneal complications early injection of **antitoxin** is most efficacious, and it is necessary carefully to avoid all procedures which may disturb the integrity of the epithelium either chemically or mechanically. If ulceration occurs antitoxin should be administered again and may be repeated daily if necessary. Careful irrigation with mild antiseptics and instillations of 1:2000 **methylene blue** should be given, and after the acuity of the attack collyria of **atropine** and of **pilocarpine** may be employed. G. Sourdille (Gazette médicale de Nantes, No. 40, p. 781, 1905).

**Diphtheria antitoxin** in the treatment of purulent conjunctivitis which, while membranous in character, was not due to the Klebs-Löffler bacillus. The first case reported by the writer was in a child aged 3 years in whom the ophthalmia was intense, involving both eyes, with great swelling of the lids, abundant purulent discharge, and false membranes covering the conjunctivæ. When the usual remedies failed Fromaget suspected a diphtheritic infection and injected a dose of 10 c.c. (2½ fluidrams) of the serum. On the following day the child opened its eyes and the cure was complete forty-eight hours afterward. Yet the bacteriological examination showed that the infection was due to pneumococci. In a second case the patient was a newly born infant with a pseudomembranous conjunctivitis. Within a few hours after the injection of the serum an ulcer was discovered in the lower part of the cornea. Within two days the swelling and the false membranes had entirely disappeared. The ulceration had begun to heal and the purulent discharge had disappeared. On examining the ulcer it was found that

it was due to the pneumococcus associated with the streptococcus. The author concluded that antidiphtheritic serum should be used in all cases that are accompanied by the formation of false membranes, whatever their bacterial origin may be. Fromaget (*Semaine médicale*, Nov. 27, 1907).

In a child of 2 whose left eyelids were swollen and hard, and the under surface was covered with false membranes, observed by the writer, nothing but staphylococci could be grown from the latter or the nasal secretions. Two days later, however, the child's condition grew worse and diphtheria bacilli were then found in pure cultures. Antitoxin was then injected in small doses, 3 c.c. on alternate days, to ward off any tendency to anaphylaxis, and recovery was soon complete. The other eye stayed normal. DaRocha (*Brazil Medico*, July 8, 1916).

### TUBERCULAR DISEASE OF THE CONJUNCTIVA.

**SYMPTOMS.**—Tubercular disease of the conjunctiva may either present itself as a primary or a secondary manifestation; in either event it is an extremely rare disease. In both varieties the disease occurs in the form of small, yellowish-gray nodules on the palpebral conjunctiva. These break down and form ulcers with uneven and indurated edges. The floors of these ulcers have either a lardaceous appearance or are covered with grayish-red granulations. The conjunctiva is swelled and turgid, the lids are thickened, and there is considerable discharge. The bulbar conjunctiva and the cornea may become affected, and in severe cases the ulcers on the palpebral conjunctiva may burrow down and involve the entire thickness of the lid. Although this gives a clinical picture which is almost characteristic, the diagnosis may be verified by the discovery of the tubercle bacillus in the contents of the ulcers.

The disease usually affects but one eye, and occurs almost without exception in the young. It manifests a great tendency to recur, and may become the starting-point of general tuberculosis.

Case of tuberculosis of the conjunctiva occurring in a patient aged 13. A congenital pigmented growth was removed from the conjunctiva and microscopic examination showed it to be a pigmented papilloma. About two weeks later the site of operation showed an elevated, red area, which increased in size and showed small foci of ulceration. Sections of this growth, examined microscopically, showed tubercles. General and local treatment gave no results. Diagnostic use of tuberculin gave positive reaction and the therapeutic use of tuberculin was followed by marked improvement. L. C. Peter (*Arch. of Oph.*, May, 1912).

**ETIOLOGY.**—As a rule, tubercular conjunctivitis is a primary disease and originates in a direct infection of the conjunctiva. When the disease occurs as a secondary manifestation, it is usually transmitted from the nasal or pharyngeal mucous membrane by means of the lachrymal passages.

Tuberculosis of the conjunctiva, either primary or secondary, is quite rare, as shown by the statistics of different authors. Eyre observed 1 case in 3000 patients affected with ocular disease, Hirschberg 1 in 6000, Bock 1 in 10,000, Lagrange 2 in 15,000, Milliga. 1 in 20,000, Mules 1 in 33,000. The writer himself has observed 3 cases in 49,000 patients treated at the Rothschild Foundation of Geneva during the past eleven years. The total number of published cases is 140 to 150 as a maximum, of which only 80 or 90 have been proved. As to primary tuberculosis of the conjunctiva only 24 cases are known in which the disease was proved experimentally or by the presence of the bacillus, and in which the integrity of the other organs was well

established. The writer reports 2 cases of the primary form, of which 1, aged 5 years, died from cerebral tuberculosis, while the other, aged 12 years, was cured. His conclusions are: (1) that tuberculosis of the conjunctiva can give rise to cerebral tuberculosis; (2) that the prognosis of the ulcerative form is graver than that of the other clinical varieties; (3) that primary tuberculosis of the conjunctiva may show lengthy remissions; (4) that primary tuberculosis of the conjunctiva is curable. Gourfein (*Archives d'ophtal.*, Sept., 1906).

Tuberculosis of the conjunctiva is an infective granuloma of the conjunctival tissues, either bulbar or palpebral, which is due to the local multiplication of the tubercle bacillus and to the action of its toxins. The frequency of the condition as seen by the ophthalmologist is about 1 in 2500.

The writer recognizes the following clinical types: 1, ulceration; 2, miliary tubercle; 3, hypertrophic granulation; 4, lupus; 5, pedunculated tumor. As the condition in one or another of its forms is closely simulated by a variety of other affections, the presence of the tubercle bacillus is an essential factor in the positive diagnosis. Tuberculin may be of diagnostic value and the best results for this purpose are to be obtained by the ophthalmoreaction of Calmette. This is limited to such cases as have the disease confined to one eye. Estimation of the opsonic index of a series of samples of the sufferer's blood gives valuable information in some cases of doubtful diagnosis. The etiological factors other than the bacillus are chiefly a family or personal history of tuberculosis. Age and sex have some slight influence.

The eye may also become involved by direct extension by continuity of surface from pre-existing tuberculous lesions (lupus), direct inoculation of the conjunctiva, or through endogenous or hemic sources. Eyre (*Lancet*, May 18, 1912).

**TREATMENT.**—This should consist in the removal of all the diseased structure if the process be localized, by the curette, knife, or galvano-cautery; but, if the involvement of the ocular structure be disseminated, enucleation should be instantly performed.

Case of tuberculosis of the conjunctiva occurring in a girl aged 4 years which was cured by the use of the X-rays. The disease had lasted two months. The palpebral conjunctiva was bestrewn with miliary granulations and folds of cockscomb-like tissue. The submaxillary glands on the same side were enlarged. Tubercle bacilli were found in sections of the granulations, and inoculation into a rabbit's eye resulted positively. The affected conjunctiva was exposed to the X-rays at a distance of six to ten inches from the focus tube, for an average period of ten minutes at each sitting. Nine such exposures were made in the course of a month, when the conjunctival malady was practically cured. The enlarged glands, however, became larger and were eventually removed. Stephenson (*Brit. Med. Jour.*, June 6, 1903).

When the tuberculous process in the conjunctiva is not too large for radical extirpation it should be excised into sound tissue. If the process is too large for this, but has not yet invaded the bulbar conjunctiva, it should be treated with phototherapy. If this is impossible on account of the extension of the process, tuberculin treatment is justified. The actual cautery, curetting, etc., may be useful adjuvants, but cannot be relied on for the whole treatment. In several cases various measures had been tried, but without results, until the process was finally arrested and the patients cured by excision into sound tissue. The results of this were always so good that he urges its general adoption as the standard procedure. Lundsgaard (*Jour. Amer. Med. Assoc.*, from *Hospitalstidende*, vol. xlviii, No. 39, 1906).

Case of primary tuberculosis of the right upper lid in a medical student from Argentina. The eye had become infected at a necropsy, pus squirting into this eye as a tuberculous cavity was incised. After **curetting** twice, systematic **exposures** to the direct **sunlight** were begun, the patient turning back first the upper and then the lower lid and exposing them in turn to the direct sunlight for a few minutes and then for a time with the eyes closed. The sittings were gradually lengthened until six or ten minutes each were given during the day, supplemented by a local sun bath for a secondary cervical lymphadenitis.

After a period of three months the tuberculosis seemed to be entirely cured, and there has been no sign of further trouble during the six months since. Rollier and G. Borel (*Revue méd. de la Suisse Romande*, April, 1912).

In a series of cases of ocular tuberculous manifestations excellent results were obtained by the writer from the use of **tuberculin** in graded doses. It caused apparent cure or marked improvement in 5 cases, including 2 of phlyctenular conjunctivitis. R. B. Metz (*Cleveland Med. Jour.*, Sept., 1916).

### **INFECTIOUS CONJUNCTIVITIS (PARINAUD'S CONJUNCTIVITIS).**

Frequently designated as Parinaud's conjunctivitis, Parinaud having first described the disease in 1888.

**SYMPTOMS.**—The first symptoms are those of a mild case of granular or purulent conjunctivitis. The secretion is not very abundant, the lids are swollen, the conjunctiva thickened, and granulations appear, which are at first small and semitransparent, then become yellowish, and, later, red and opaque. In most cases some of the granulations assume a polypoid character, and may attain one-quarter of an inch or more in

length. These granulations, hanging chiefly from the fornix, present a most striking appearance, and form one of the characteristic features of the disease. If the granulations be separated with a probe small erosions will be found lying between them, as well as minute, yellow granules, which resemble those seen in tuberculosis of the conjunctiva.

The bulbar conjunctiva is injected and often edematous. The cornea is unaffected, and the disease is almost always confined to one eye. Shortly after the ocular symptoms manifest themselves, although in a few cases preceding them, preauricular and parotid glands, and at times the submaxillary and retromaxillary glands of the same side as the affected eye, become swollen and indurated, and not rarely break down and suppurate.

The organism at large invariably shows signs of depression, and there is some fever throughout the course of the affection; its onset may be inaugurated by a distinct chill. The disease is essentially chronic, both ocular and granular symptoms persisting and resisting treatment for weeks and months, though if left to itself it will undergo spontaneous cure without leaving scars in the conjunctiva. But little pain is experienced, either from the swollen lids or the enlarged glands. The disease is non-contagious.

**DIAGNOSIS.**—The symptoms of the disease are so striking that it cannot readily be confused with any other form of conjunctivitis, except, perhaps, tuberculous conjunctivitis. It simulates this latter disease very closely, and, though the simultaneous involvement of the glandular system, and the peculiar pedunculated character of the granulations in some cases, and the rather char-

acteristic erosions which occur between the granulations will usually enable the diagnosis to be made from tuberculous conjunctivitis without any great difficulty, yet in other cases the result of histological examinations and of experimental inoculations will have to be obtained to make the differentiation absolute. Though bearing a certain resemblance to trachoma, it can easily be differentiated from that form of conjunctivitis by the more diffuse character of the infiltration, the length of the granules, the non-affection of the cornea, and the involvement of the glandular system.

Necessity of differentiating Parinaud's conjunctivitis from other forms of conjunctivitis. It is not contagious, and it is impossible to reproduce the affection in animals. In man it runs a relatively mild course, healing in from seven to ten months without leaving any trace. The cornea and the lachrymal passages persist intact throughout its entire course. The assumption of an animal origin is problematic, he continues, and the affection is not tuberculous. The chief characteristics are the inflammation and granulations, the swelling of the lids, the infarct in the lymph-nodes and the fever and anorexia—no other form of conjunctivitis combines these four groups of symptoms. Diphtheria antitoxin injections seem to modify favorably the primary stage of the disease, but he warns expressly against cauterization of the granulations, as this is liable to leave complications in the cornea, while, left alone, the lesions subside in time completely. The *Bacillus xerosis* seems to have something to do with the affection. He reports in detail 3 cases in children and 1 in a brother physician. R. Arganaraz (Semana Medica, April 4, 1912).

**ETIOLOGY.**—The origin of the affection is still unknown. Parinaud thought that it originated from decayed

animal matter, and termed it "infective conjunctivitis," but, as this observation was based solely upon the coincidence of the disease originating in some of the cases observed by him in subjects who were more or less exposed to infection of such a source, and though a possibility of infection under similar conditions has been reported by others, the bacteriological proof of this, though carefully and repeatedly searched for, has not been found.

From 5 cases of an epidemic of conjunctivitis in an institution the writers have obtained in each case a pure culture of a Gram-positive diplococcus, with elongated and lancet-shaped elements. The superficial examination ordinarily employed in ophthalmic practice is insufficient to distinguish it from the pneumococcus, from which it really differs markedly. J. P. McGowan and W. Macrae Taylor (Lancet, Nov. 11, 1911).

Verhoeff and Derby conclude that the theory of animal origin is grounded upon insufficient evidence, and that the agent which produces the local lesion is non-pyogenic, and that suppuration, if it does occur, is probably due to secondary infection. They regard Parinaud's suggestion of foot-and-mouth disease as the source of the infection as purely hypothetical, although they mention as a rather striking fact that Parinaud's conjunctivitis has been reported only in France and America, countries in which foot-and-mouth disease is especially prevalent. They state that, moreover, five of the American cases occurred in cattle-raising sections, and one in Boston, a seaport from which cattle are exported in great numbers. Stirling and McCrae found pure cultures of bacillus resembling Klebs-Löffler bacillus, which led them to conclude that they were dealing with either a virulent form of

*Bacillus xerosis* or one less toxic than ordinary *Bacillus diphtheriæ*.

**TREATMENT** consists in antiseptic lotions and cauterization with **silver** or **copper**. When the granulations are large, **excision** may be practised, and when the disease is very chronic, and the swelling of the lids extreme and resistant, searing with the **actual cautery** may be necessitated. **Alterative ointments** should be applied to the affected glands; if suppuration threatens, **hot compresses**, followed by **incision** and **drainage**.

The treatment of Parinaud's conjunctivitis consists of **nitrate of silver**, **copper sulphate**, a **bichloride** application, and **incision** or **expression** of growths. Two personal cases:—

CASE 1.—Mrs. H. S., 52, wife of a farmer, came with an eye red, chemotic, marked granulations, hazy cornea, and enlargement of the preauricular and cervical lymphatics. It varies from the usual description in the involvement of the cornea. The treatment was **atropine**, **argyrol** 5 per cent., and **silver nitrate** 2 per cent. In six months the lids were better, but the cornea persisted cloudy.

CASE 2.—L. H., 4. Right eye. Inflammation of lower lid with granulations, slight chemosis, preauricular and cervical glands enlarged. In two weeks the upper lid became worse. Ulcers formed on the lids. Treated with **argyrol** and sometimes **atropine**. Two glands had to be opened to evacuate pus. The patient was better, but not recovered, at the time of writing. R. M. Lapsley (Ophthalmology, Oct., 1911).

## LUPUS OF THE CONJUNCTIVA.

Conjunctival ulcers occurring in this disease are distinguishable from tubercular ulcers chiefly by the fact that they have involved the conjunctiva from the skin, instead of from the mucous mem-

brane, and, like cutaneous lupus, they undergo spontaneous healing in one place, while the ulcer keeps advancing in another. The disease occurs either as a primary process or as an extension of the disease from the surrounding skin. It appears as an ulcer, the bottom of which is covered with granulations, which bleed on the slightest touch and are filled with tubercle bacilli.

Treatment consists in thorough removal of the contents of the ulcer with a **curette**, followed by careful **cauterization**.

## PEMPHIGUS.

Pemphigus of the conjunctiva is a very rare affection, and is usually seen in connection with pemphigus vulgaris of other parts of the body, although it may occur as an independent disease. Bullæ form upon the conjunctiva and are attended with pain, photophobia, and lachrymation. The blisters break down and form cicatrices in the conjunctiva. Repeated recurrence is the rule, so that the membrane finally becomes much shrunken and atrophied, and appears dry, smooth, and tense. The cornea becomes cloudy and the lids are frequently distorted, aggravating the symptoms by the displacement of the cilia which this occasions.

Treatment is of no avail, though the condition may be mitigated by **emollients**, and protection from the light and air by **coquilles**. **Arsenic** may be administered internally.

Case of pemphigus of the conjunctiva, the progress of which was very rapid and destroyed the vision of both eyes in about three months. The disease was limited at first to the conjunctiva, but later the characteristic eruption appeared on the body. This primary appearance of pemphigus on the conjunctiva had been known to occur before, but it

was rare. The etiology of the disease was obscure. Some writers believed it neurotic, some that it was trophoneurosis, some that it was an affection of the nerve-endings by toxins. In the case reported both Wassermann's and von Pirquet's tests were negative. No surgical measures were employed in the treatment. All local treatment was usually unsuccessful, although occasionally grafting succeeded. In its early stage the disease was mistaken for trachoma. W. B. Weidler (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 8, 1912).

### SYPHILITIC DISEASE OF THE CONJUNCTIVA.

Chancres about the eye, as a rule, develop on the edge of the lids; they may also be observed on the palpebral conjunctiva and rarely on that of the globe. The disease is usually transmitted by kissing. At times, however, ulcers may form from the breaking-down of gummata of the conjunctiva.

### TUMORS OF THE CONJUNCTIVA.

Tumors of the conjunctiva may be both malignant and benign.

**Dermoid.**—The most common among the latter is the dermoid, which is always congenital and is often found associated with wart-like growths from the skin in front of the ears, and with harelip. They are ascribed to an arrest of development. They occur as pale-yellow, rounded or oval bodies, the size of a split pea, usually at the extreme limbus of the cornea. Their surface is dry and smooth and frequently has a few hairs projecting from it.

If, as sometimes happens, the growth shows a tendency to involve the cornea or to cause irritation, it should be **excised**, care being taken to avoid injuring the deeper layers of the cornea.

**Polypus** is a benign, pediculated growth of the conjunctiva, which is but rarely seen. It is usually very small and is found in conjunction with the caruncle.

**Papillomata** are occasionally confounded with polypi, but may be readily distinguished from them by their rough, raspberry-like surface. They may be pediculated or sessile. Both forms of growths may be readily **removed** with scissors.

**Angiomata** are rare, but when they occur are usually found in association with a caruncle. They are congenital, but, as they usually increase in size after birth, their **removal** is usually demanded. (See also Blood-vessels, Tumors of, Vol. II.)

Case in which the **injection** of 2 or 3 drops (0.12 or 0.18 c.c.) of absolute **alcohol** caused the injected portions to assume a pale grayish-pink color, and after a week or ten days the tumor was much reduced in size. The injections were then repeated, the needle being carried part of the time one-half inch into the orbit. After this, alcohol was injected every two or three weeks for the next two months; at the end of this time the original tumor had practically disappeared, but now the conjunctiva from the outer third of the corneal margin to the external canthus, which had seemed normal, became dark red, and, fearing an extension of the growth around the deeper portions of the globe, more alcohol was injected, three-fourths of an inch deep, along the inner wall of the globe and half an inch deep into upper and lower fornices. After this the improvement was steady, and when the patient went home there was no tumor visible, and the only trace of the former trouble was a moderate congestion of the inner half of the conjunctiva, which was steadily improving. Gifford (Ophthal. Record, Dec., 1906).



The conjunctiva is rarely the seat of malignant tumors, but both epithelioma and sarcoma may occur. They both arise from the tissue at the limbus.

**Epithelioma** of the conjunctiva is non-pigmented, and occurs as a flat, reddish tumor, with a broad base. The tumor slowly increases in size, involving the cornea like pannus, and is prone to ulceration.

**Sarcoma** is usually pigmented and may attain large size, the growth being at times very rapid. They rarely attack the cornea.

The early removal of both of these forms of growth is imperative, to prevent implication of the other structures of the eye. **Enucleation** is frequently demanded.

**Cysts.**—Simple cysts of the conjunctiva are very uncommon. They appear as translucent, spherical bodies the size of a pea, usually on the bulbar conjunctiva, and may be regarded as dilated lymphatic vessels.

**Cysticercus.**—Subconjunctival cysticercus is also an extremely rare affection. It may be distinguished from the foregoing by the fact that it may be readily moved under the conjunctiva, while simple cyst cannot, as a rule, be moved from its position. The diagnostic point, however, is the presence of a round, white, opaque spot on the anterior surface of the tumor, the receptaculum of the cyst. **Excision** of the growth by dissection is indicated.

Among the congenital tumors of the eyelids there exists a variety that is very rare, if we may judge from the silence of authors on the subject, which the writer denominates an "embryonal conjunctivoma." The clear cells of which it is composed may undergo liquefaction in the center of the mass and give place to the formation of a seroalbuminous cyst

which can be distinguished from the congenital mucous cysts of the lid. The prognosis of a "pure conjunctivoma" is good; it does not recur after extirpation. Letulle (*Presse méd.*, Nov. 21, 1908).

## MISCELLANEOUS DISORDERS OF THE CONJUNCTIVA.

**Conjunctival Ecchymosis.**—This may be originated by traumatisms or violent inflammation of the conjunctiva, or may occur spontaneously in the aged, from brittle blood-vessels, and in children in association with disease attended by spontaneous hemorrhage elsewhere, particularly after whooping-cough.

The meshes of the conjunctiva become filled with blood, and the staining of the tissues may persist for some weeks. When the ecchymosis appears under the conjunctiva several days after an injury to the head, it becomes an important factor in the diagnosis of fracture of some of the bones composing the orbit.

**Chemosis.**—Chemosis of the conjunctiva results when the connective-tissue layer is filled with serum, usually as the result of a severe inflammation of the conjunctiva or some of the deeper ocular tissues; it may, however, appear spontaneously.

**Lymphangiectasis** of the conjunctiva occurs at times as a small collection of blisters on the bulbar conjunctiva, due to distention of the lymph-channels as a result of interference with their circulation. It may occur at any stage and is not significant.

**Lithiasis** of the conjunctiva consists in the deposit of chalky matter in the ducts of the Meibomian glands, and gives the appearance of numerous, small, yellowish-white spots scattered throughout the conjunctiva. As they frequently

occasion considerable irritation, they should be removed by incision.

Case of conjunctivitis petrificans in a female aged 30 who presented irregular opaque areas situated in the conjunctiva under the epithelium and projecting but little above the surface. There were but few symptoms of irritation, and these were scanty secretion, with a tendency to spontaneous disappearance without leaving any trace in the early stages. The treatment consisted in carefully dissecting out many of the chalky areas, in the employment of a boric wash and of a solution of atropine. W. C. Posey (*Annals of Ophthalm.*, April, 1905).

**Amyloid disease** of the conjunctiva is due to a peculiar degeneration of the conjunctiva in which pale-yellowish masses appear chiefly on the palpebral conjunctiva, but also in the bulbar portion. The lids become much swelled without the usual attendant signs of inflammation. The conjunctiva resembles white wax.

The disease is primary, although it may also at times be developed from granular conjunctivitis.

Treatment should consist in removing sufficient of the conjunctival masses to permit of greater freedom in the movements of the lids, which are often much restricted, and to gain better vision.

**Pinguecula** is a small, yellowish elevation in the bulbar conjunctiva near the corneal limbus, and usually situated to the inner side. It is composed of connective tissue and elastic fibers, in association with a colloid substance; it is due to the action of external irritants. It has no significance beyond its cosmetic effect, except that it may originate pterygium.

### **PTERYGIUM.**

**SYMPTOMS.**—Pterygium consists in a triangular fold of hypertrophied

conjunctival and subconjunctival tissue of fleshy appearance, generally situated to the inner side of the cornea in the palpebral fissure. It may, however, be on the outer side of the cornea, and in the traumatic variety may entirely surround the membrane. The apex of the triangle or the head of the growth is attached to the cornea, while the base spreads out like a fan into the semilunar fold. The neck of the growth lies between the apex and the base, and corresponds to that part which lies on the limbus.

At times the pterygium may push its way across the cornea and disturb vision by involving the pupillary area of that membrane. But usually, however, it shows no tendency to advance into the cornea.

In its early stages the growth is thick and fleshy in appearance; but it becomes paler after a time and its blood-vessels are reduced to fibrous cords, giving the structure a tendinous appearance.

Pseudopterygium may always be diagnosed from the true variety by the fact that a probe may be passed under the neck of the latter, whereas this procedure is impossible in pseudopterygium, owing to the matting together of the tissues by the preceding inflammation.

**ETIOLOGY.**—Pterygium never occurs in children, although it is not an uncommon disease of adult life. Fuchs thinks that its starting point is usually a pre-existing pinguecula, and that it is due to the prolonged influences to which the conjunctiva in the region of the palpebral fissure is exposed. It is especially common among persons who are submitted to the inclemencies of the weather: sailors, coachmen, farmers, and others.

Pseudopterygium, or traumatic pte-

rygium, occurs as a result of some inflammatory process which causes a lesion of the margin of the cornea. This variety is especially liable to form after burns or marginal ulceration occurring in purulent conjunctivitis or phlyctenular disease.

Pterygium and pinguecula are often the result of irritation from the presence of fine, downy hairs on the inner side of the lids. A cure can be effected by removal of the hairs. The latter are generally found in the inner angle; in some cases the writer has found them so long that they projected 2 mm. beyond the limbus of the cornea, but they are so fine that they can seldom be seen without a magnifying glass. Series of 6 personal cases. In an examination of 1100 inmates of an insane asylum he found the hairs in all but three of the individuals affected with pinguecula, and in nearly all the cases of progressive pterygium. The stationary, traumatic cases, of course, do not belong to this category. Sachsalber (Wiener klin. Woch., Bd. xviii, Nu. 29, 1905).

**TREATMENT.**—If the pterygium be small and shows no tendency to involve the cornea, it should be allowed to remain, for its removal for cosmetic purposes will be unsatisfactory owing to the scar which remains upon the cornea and conjunctiva.

A pterygium may be removed either by **excision** or by **ligature**. In the former method the **operation of McReynolds** is preferred. The head of the growth is grasped with fixation forceps and cut smoothly from the cornea by a sharp knife. The lower border of the pterygium is then divided from the conjunctiva, and the growth forced from the underlying tissues. The conjunctiva below the mucosa is then undermined and the pterygium buried under it, by

carrying a black-silk thread around at each end with small needles through the apex of the pterygium and bringing them out from under the conjunctiva into the lower fornix, where they are tied. If the growth be very large, it may be split into an upper and lower half after its dissection from the cornea, and the flaps thus obtained transplanted into the superior and inferior *culs-de-sac*.

A simple procedure in the treatment of pterygium described by A. Coe was **cauterization** of the head of the membrane by means of a platinum wire, with a fine bulbar end, not larger than a very small pea, and heated in an alcohol-lamp. Practically complete cure was obtained by the writer in an extensive pterygium by three cauterizations of this kind, carried out at intervals of a few days. At the end of several months it was possible to make out only a light opacity, corresponding with the thickening in the conjunctiva, while the nearer tissues were entirely transparent. The same treatment in 24 cases invariably gave good results, excepting in 1 patient, who presented a very extensive pterygium with large vascularities. F. B. Loring (Semaine méd., No. 34, 1902).

## INJURIES OF THE CONJUNCTIVA.

**Foreign Bodies.**—Small-sized foreign bodies frequently make their way into the conjunctival sac and cause considerable pain by the pressure which they exert upon the cornea with every movement of the lid. If the body be found imbedded in the lower *cul-de-sac*, it is an easy matter to remove it, but if it be under the upper lid it is necessary to evert the latter. This is accomplished by grasping the lashes and the edge of the lid with the thumb and forefinger of the right hand while the patient is directed to remain looking down, slightly

pressing upon the upper edge of the tarsus either with a finger of the other hand or some convenient instrument: a blunt pencil, a probe, etc.

Two cases in which rather severe reaction followed an apparently simple accident. While sharpening an indelible pencil a particle of the point lodged on the conjunctiva. Considerable smarting and lachrymation followed, but in a short while the pain subsided and the only discom-

Large bodies may remain buried deep in the *culs-de-sac* for weeks at a time, and merely cause the symptoms of a chronic catarrhal conjunctivitis. Of this nature is the inflammation set up by the "eye-stones" which are frequently introduced into the eye by laymen to remove cinders or other foreign bodies. Having performed their function, they become imbedded in the folds of the conjunctiva.

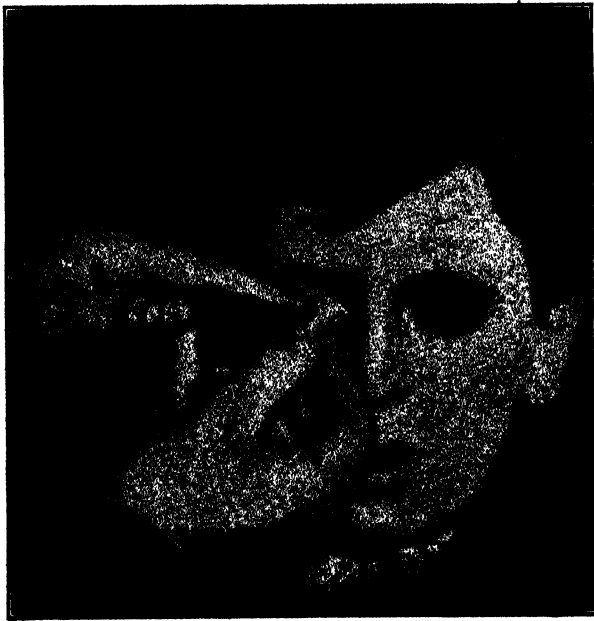


Fig. 1.

fort felt was the excessive lachrymation, which was stained a deep blue. Later the lids became much swollen and edematous, and there was considerable photophobia. The corneal epithelium was colored blue and so steamy that only a blurred iris could be seen. In one case a large ulcer formed, involving the cornea and conjunctiva and extending into the upper *cul-de-sac*. The conjunctiva, in addition to being stained and thickened, also presented a peculiar dry appearance and was partly anesthetized. J. M. Ray (Ophthal. Record, Jan., 1905).

When the foreign body is minute, and difficulty is experienced in detecting it, direct the patient to move the eye in various directions so as to vary the background; this will facilitate localization, since the black of the pupil will form a favorable contrast if the particle happens to be of light color, such as ashes, and the iris a good background if it is of the more usual dark tint. This procedure also enables one to seek the foreign body from different angles, and makes detection more certain.

If nothing is discovered upon the cornea, the conjunctiva of the upper

lid must be explored. It is comparatively easy to turn the upper lid if the following directions are observed: The patient must look downward; the lashes of the upper lid at about its center are now grasped firmly between the thumb and index finger of the operator's right hand and the lid thus pulled downward (Fig. 1); the end of the index finger of the left hand, or a probe, is then placed on the external surface at a point cor-

per cent. solution, **alypin** in 3 per cent. solution, or **novocaine** in 3 per cent. solution may be used; of these three the writer prefers **holocaine**, because the anesthesia is more profound, but **alypin** and **novocaine** are also satisfactory. Solutions of cocaine muriate are inferior and open to objections. It is necessary to use more than 1 drop of the local anesthetic; instill a drop, after two minutes another, and two minutes later

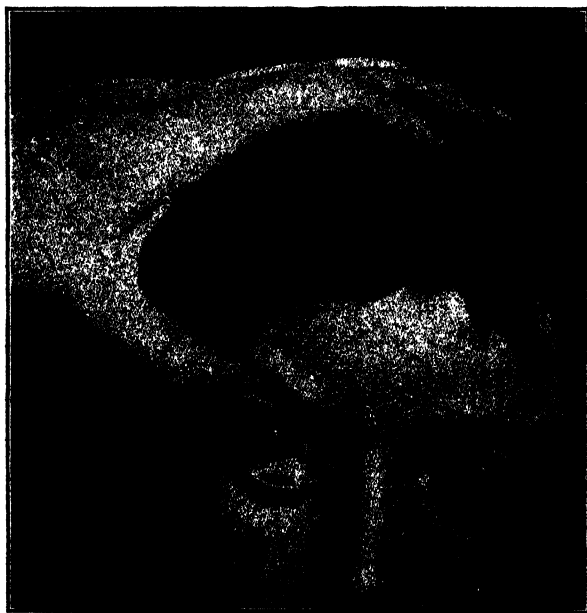


Fig. 2.

responding to the upper border of the tarsal cartilage and used as a fulcrum upon which the eyelid is suddenly turned; having turned the lid, it is kept everted during the process of illumination and searched by the thumb of the left hand, the extended fingers resting upon the patient's forehead and parietal region. (Fig. 2.)

Having located the foreign body, the next step is to anesthetize the eye, thus facilitating the removal of the offending material and avoiding pain to the patient. The local anesthetics which are best employed for this purpose are substitutes for cocaine—either **holocaine muriate** in 1

a third and final drop; after waiting a few minutes longer the eye is ready. It must be remembered that all local anesthetics, and especially all the substitutes for cocaine, cause a slight burning sensation and irritation which pass off within a few minutes.

If nothing be found either upon the cornea or the under surface of the upper lid, and we have reason to believe that a foreign body is still lodged upon the cornea, it may be well to instill a drop of **fluorescein solution** (2 per cent. fluorescein and 3 per cent. sodium bicarbonate in water); small ophthalmic disks con-

taining these ingredients are convenient for this purpose. This reagent is allowed to remain with closed lids for two minutes and then the excess is washed away with boric acid solution; the pigment has the property of staining an abrasion of the cornea, and of causing a small green ring around a foreign body, and thus a minute particle which may have defied discovery in the ordinary manner will be detected quite readily.

the upper lid exactly at its margin and push upward; then apply the end of the index finger firmly to the lower lid, and push downward; at the same time press backward slightly (Fig. 3); do not touch the eyeball with the nails of the fingers used as separators. In this manner the lids will be kept apart and the eyeball will be fixed so that its cornea cannot be rotated out of view, an inclination which the patient finds

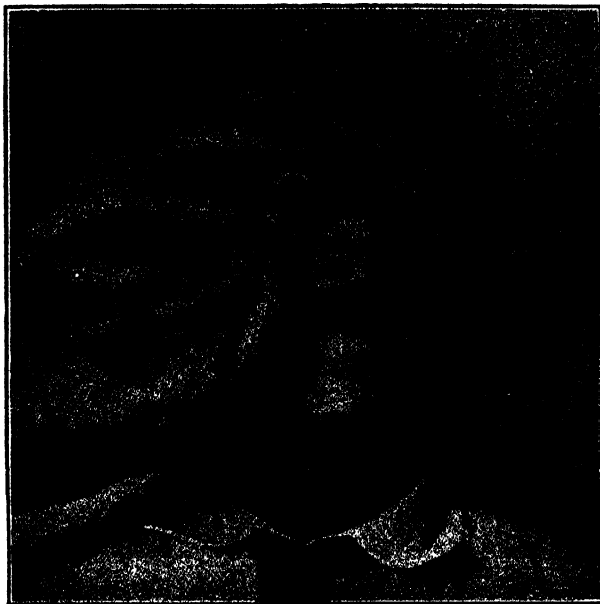


Fig. 2.

Very few individuals have sufficient control over their eyes to keep the lids open and calmly allow the operator to remove the foreign body; instinctively the patient will close the lids whenever he sees the approach of the instrument with which the cinder is to be removed. Hence it will be necessary, in most cases, to hold the lids apart and at the same time to steady the eyeball. This is done in the following manner: Request the patient to keep both eyes open; he will resist less if he does this than if he attempts to close the non-affected eye. Apply the end of the middle finger of the left hand to

difficulty in resisting under the circumstances.

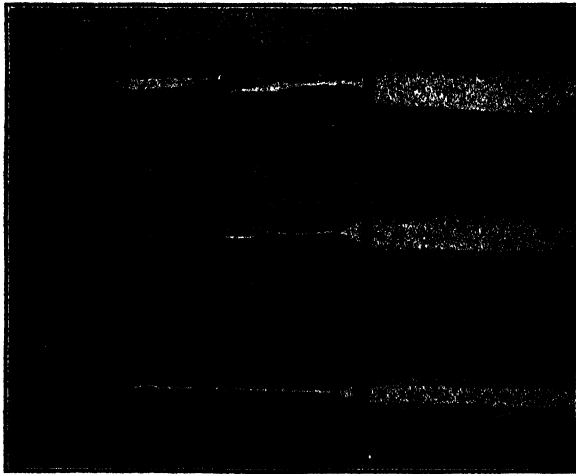
It is well to remember that most foreign bodies are attached lightly to the cornea; often they become more deeply imbedded because the initial procedure in removal has been faulty or too rough. Start with the idea that the foreign body is loosely adherent. In order to dislodge it use a small cotton applicator or a blunt foreign-body spud (Fig. 4) around the end of which a small tuft of absorbent cotton has been wound. Commence by trying to brush off the foreign body; if this does not succeed, wind the cotton

more firmly upon the applicator or spud and endeavor to push it off; these procedures will be sufficient in most cases, and if successful will avoid unnecessary wounding of the cornea. In brushing the cornea do not be content to apply the force in one direction only; if the first attempt is not successful, vary the maneuver by brushing from other or different directions.

It is only after these light procedures have been unsuccessful that we should have recourse to scraping, lifting, or digging efforts. If the

avoid unnecessary injury to the cornea, and when sharp instruments are resorted to the danger of perforation must be kept in mind.

If a particle of iron or steel seems to have penetrated the greater part of the thickness of the cornea, it should be loosened with the foreign-body gouge or needle, and then it can easily be extracted with the magnet. If such a foreign body is very firmly and very deeply imbedded in the cornea it will be wiser for the general practitioner to desist and not to attempt its removal, but to leave



Figs. 4, 5, 6.

cotton-tipped applicator has not dislodged the foreign body we should resort to the spud, and, since it should be our endeavor to give relief with the instrument which causes least damage to the cornea, we commence with the blunt spud; this and all other instruments used must be well sterilized; we should attempt to scrape off the foreign body, and generally this will succeed. If not, the semisharp spud, known as the corneal gouge (Fig. 5), may be employed, and scraping, digging, or lifting resorted to; in certain instances the foreign-body needle (Fig. 6) may have to be used. In every case the amount of force must be as gentle and as limited as possible, so as to

this for the ophthalmologist; in such instances it will be necessary to take precautions to guard against perforating the cornea and pushing the foreign body into the anterior chamber. If the piece of metal has penetrated the entire thickness and is sticking in the cornea, a broad needle is passed into the anterior chamber and pressed from behind forward against the foreign body, so that the latter cannot escape into the anterior chamber during the process of extraction.

It is always a mistake to leave even the smallest trace of a foreign body in the cornea, since such minute portions give rise to a great deal of irritation and cause as much

trouble or more than if the foreign body had not been interfered with at all. Such remnants are often eventually loosened by an ulcerative process and thus finally escape; but in the mean while the patient suffers much discomfort, the eye becomes irritated, congested, and exposed to the danger of infection.

If a particle of iron or steel has been allowed to remain upon or in the cornea for a day or two or longer it will become surrounded by a ring

patient should be instructed to flush the eye with a dropperful of boric acid solution every hour until the irritation has subsided.

If the foreign body is beneath the upper lid it is usually easily brushed off after the lid has been everted; it is rarely, if ever, necessary to use the naked end of the foreign-body spud or gouge for this purpose.

We are sometimes unsuccessful in finding any foreign body, and this will mean either that it has escaped



Fig. 7.

of rust; this area must be removed with the fragment of metal by scraping or else the irritation will continue.

It is wise to inform the patient that the eye will feel sore for some hours after the removal of the offending particle, if the latter has imbedded itself at all into the corneal epithelium, since the effects of the local anesthetic soon wear off. No matter how delicate and gentle the operator has been the removal of a foreign body from the cornea by means of the blunt or sharp spud or needle will leave a wound, and the latter will cause some pain or irritation until it has healed. With proper care this will be a clean wound; in order to prevent subsequent infection the

previous to the time at which the patient presented himself, or that it has been removed with the manipulation necessary to examine the eye, or that it is one of those rare instances in which it has lodged in the retro-tarsal fold. To expose the latter (Fig. 7) turn the upper lid as directed above, the patient continuing to look downward; next press the edge of the everted upper lid firmly against the supraorbital margin with the thumb of the left hand; then push the lower lid upward over the cornea with a finger of the right hand, at the same time exerting gentle backward pressure upon the eyeball. Charles H. May (Amer. Jour. of Surg., June, 1912).



**Wounds.**—The conjunctiva is not infrequently involved in wounds of the globe itself or of its adnexa. If the wound be extensive, the edges should be approximated with stitches, but otherwise a simple **boric acid wash** with a **protective bandage** will suffice.

**Burns.**—Burns of the conjunctiva are common. These are usually caused by lime, acids, hot water, hot ashes, molten metal, etc., and are particularly serious on account of the subsequent contractions and deformities which they occasion in the lids and damage wrought in the cornea.

Burns of the eyelids and conjunctiva, especially by lime, are of frequent occurrence, and ~~the~~ practitioner may be called upon to treat them. It has long been known that a saturated solution of picric acid is one of the best applications to a skin burn, relieving the pain in a marvelous manner and acting as a powerful antiseptic. After making experiments with rabbits' eyes and after long clinical experience, the writer warmly recommends **picric acid** for treating burns of the conjunctiva and cornea, especially by chemical agents, including lime. He finds that a 2 per cent. ointment—picric acid, 20 cg. ( $\frac{1}{2}$  grain) to white vaselin (neutral reaction) 10 Gm. ( $2\frac{1}{2}$  drams)—is better than a watery solution. He applies it twice or thrice in the day after the instillation of a few drops of **cocaine**. The results are surprising, especially in the direction of relieving pain. Symblepharon is infrequent after the picric acid treatment. A. Fortunati (Annali di Ottalmologia, vol. xxxvi, fasc. 12, 9 to 11, 1907).

If the substance inflicting the burn is lime, the eye should be washed with a diluted or weak solution of a mineral acid, or, if this be not at hand, all particles should be removed at once by forcibly **flooding** the eye with water from a hose or spigot.

Four conditions may be caused by electricity on the eyes: Traumatic electrical ophthalmia—burns of the eyelids and the globus; electrical amblyopia characterized by absence of material lesion of the fundus, by photophobia, and central scotoma; simulated amblyopia—malin-gering; saturnine (lead) amblyopia in professional electricians. As for the treatment, the author advises the wearing of **uranium spectacles**, and spraying the eyes for four or five minutes several times daily with the following:—

*Dionin* ..... 0.3 Gm. ( $4\frac{1}{2}$  grains).

*Sodium bromide* 1 Gm. (15 grains).

*Cherry-laurel*

*water* ..... 25 Gm. ( $6\frac{1}{2}$  drams).

*Distilled water*. 275 Gm. (9 ounces).

Cold compresses may also be applied to the eyes two or three times daily. Galezowski (Rec. d'Ophtalm., Sept., 1902).

If an acid has caused the burn, it should be neutralized by a weak solution of **borax**, **bicarbonate of soda**, or of **common salt** if nothing else be on hand.

Subsequent inflammation is best combated by **cold compresses**, **boric acid**, **atropine**, and some emollient substance, such as **vaselin**.

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Philadelphia.

**CONSTIPATION. —DEFINITION.**—Prolonged retention of feces in the alimentary canal; retarded defecation; a symptom resulting from a variety of morbid conditions of the intestines, and not a distinct disease. The strictly natural law governing intestinal evacuations in man requires one, and sometimes two, discharges every twenty-four hours.

**SYMPTOMS.**—The symptomatology of habitual constipation varies much in different cases. Many persons appear to enjoy fair health with

an evacuation only once in two or three days. A smaller number continue well with only an evacuation once a week; one woman came under the observation of one of us who had had no fecal discharge from the bowels for thirty days, and yet had been attending to her household duties all the time, with only a sense of fullness in the abdomen and some dizziness in her head.

Kotayya reported the case of a Hindoo aged 50 years who, since his 30th year, was in the habit of passing stools once in six months or so, and even then only two or three hard scybala were passed. But every eight months the man got a severe attack of fever, preceded by rigors, and then he passed, to his entire relief, sometimes consciously and at others in an unconscious state, enormous quantities of black, semisolid, feculent matter, which had evidently been accumulating in his intestines all the while. Notwithstanding all this, the man looked well and healthy. Classic works refer to a case in which but one movement occurred yearly.

In a large majority of persons, however, constipation causes an *auto-intoxication* of a mild type, manifested by a sense of fullness, lassitude, mental depression, or dull pain in the head, with some impairment of digestion, anorexia, pyrosis, nausea, etc., with sometimes colicky pains and distention—all of which symptoms are temporarily removed by a free movement of the bowels. In some cases after retention of the intestinal contents from three to five days, a spontaneous diarrhea supervenes for a single day, after which the constipation returns as before. Such cases are relatively common.

Attention called to the remarkable prevalence of constipation recently observed among soldiers in active service, due in part to insufficiency of green vegetables and fruit in the diet, a relatively sedentary life in the trenches, and intestinal inhibition of psychic origin. In the matter of diet the simplest prophylactic measures would consist in the addition of prunes, raisins, and "pounded" apples and pears, together with the avoidance of white bread. A. Martinet (*Presse méd.*, June 15, 1916).

The senile are often unduly convinced that they are constipated and apply all kinds of measures against it. Physicians should not be misled by their statements and complaints, otherwise a vicious circle becomes more and more established. The forgetfulness of the patient is a potent factor; he does not remember when he has been to stool and may honestly believe that days have elapsed since his last passage. Merklen (*Paris Méd.*, July 21, 1917).

In many other cases, protracted constipation leads to a violent attack of headache every week or ten days, accompanied by vertigo, *muscæ volitantes*, rapid and sometimes irregular pulse, extreme nausea or vomiting for a day, during which the bowels are evacuated, and the next day the patient returns to his ordinary duties, though pale and impaired in strength. The fact that, as shown by Herter, 126,000,000,000 micro-organisms are present in each daily stool explains these morbid phenomena, which are also due to autointoxication when retention occurs. Indicanuria is often present in these cases. Melancholia may also be due to this cause.

A true *fecal sapremia* attended by severe symptoms such as prostration, sharp abdominal pain, sustained high temperature, tachycardia, cephalalgia; a dry, furred tongue, and even an

eruption—besides all the symptoms enumerated above—may suggest typhoid fever. The character of the eruption, which is usually erythematous, generally serves to eliminate the latter diagnosis. At times, however, the Widal test becomes necessary, if the symptoms persist after the intestines have been cleared of their contents by purgation. Unconsciousness and even death have occurred where evacuation could not be obtained.

In many cases the middle and posterior parts of the tongue are covered with a light coat and the urine is deeper color and less in quantity than natural; the appetite is variable. Sometimes the colon is distended with gases, with slight tenderness on pressure and irregular peristaltic movements. In such cases the operation of a purgative is liable to be accompanied by pains across the abdomen and tenesmus, and some mucus may be evacuated with the feces. Such symptoms indicate congestion or inflammation in the mucous membrane of the rectum, which is sufficient, in some cases, to cause frequent slimy discharges, while the ascending and transverse colons remain filled with compact feces.

*Fecal colic* is apt to occur when large fecal masses accumulate in the intestine, the colicky pains being sometimes sufficiently violent to cause fainting. Distention of the abdomen by gas is usual, and temporary relief is obtained on the passage of flatus. In some cases fecal colic precedes every daily evacuation. Some cases resist purgatives and proceed until symptoms of intestinal obstruction appear with profuse vomiting and collapse. Death may even occur in old and weakened people.

Deductions of practical value can be drawn only from a study of a large number of cases. Of a group of 45 cases of spastic constipation, 24 had pyrosis before meals, the remainder no pyrosis; 27 had acid eructations from  $\frac{1}{2}$  to 2 hours after meals; 10 had vomiting and 13 nausea; and 39 had normal or increased appetite. Fluoroscopically 26 showed spastic contraction of the stomach; gastric evacuation was normal in time in 43 cases and retarded in 1; the gastric shape and mobility was normal in all; and there was more or less ptosis in only 8 cases. There was moderate hyperacidity and hypersecretion in 17; subacidity in 10; and normal acidity in 17. Abnormal amount of mucus was present in 34 cases. A positive benzidine test in 18, showed engorgement of the mucosa. W. G. Morgan (Jour. Amer. Med. Assoc., Nov. 17, 1917).

*Fecal tumors* may be formed in almost any situation; but they are, as a rule, met with in the cecum, sigmoid flexure, or rectum, causing, in most cases, more or less dislocation of the intestinal segment in which they occur, especially the transverse colon. The tumor may, as a rule, be distinctly felt on palpation as a doughy, movable mass, though in some instances it may be hard and nodular. It may attain a large size and weigh several pounds, and by producing stercoral ulcers, obstruction by kinking, owing to its weight, compression, occlusion, and peritonitis. In some cases daily evacuation may occur, owing to the presence in, or on the side of, the fecal mass of a free passage or canal.

**DIFFERENTIAL DIAGNOSIS.**—Simple retention of the fecal contents of the intestines longer than natural may be considered as sufficient diagnostic evidence of constipation in an unqualified sense. But as

undue retentions of feces are often caused by a variety of mechanical obstructions, such as strictures, invaginations, concretions, morbid growths or tumors, and visceral displacements, all these have, by common consent, been classed as intestinal obstructions, while the words "costiveness" and "constipation" are properly made applicable only to such cases as depend upon failure of one or more of the physiological conditions on which regular intestinal evacuations depend.

Differential diagnosis involves, first, proof of the absence of mechanical obstructions, and, second, proof that the physiological conditions concerned in natural evacuations are at fault in any given case. In all cases of intestinal obstruction the pains, distention, and tenderness are uniformly manifested at some one part of the abdomen or pelvis. If the obstruction is from the pressure of tumors or morbid growths, these can generally be detected by proper physical examination of the abdomen.

If from stricture or invagination there will be not only well-marked pains and fullness at some one location, but in strictures, especially, the past history of the patients will show them to have been the sequelæ of dysentery, typhoid fever, or some form of primary intestinal ulceration. Obstructions by uterine displacements or rectal concretions are readily detected by direct examinations through the vagina and rectum.

According to Kelsey, a result of chronic constipation often seen, which may not only simulate, but also cause, uterine trouble, is enlargement and pouching of the lower third of the rectum. This condition is found very frequently in virgins, and gives the

pain in the back, discomfort in standing or walking (more particularly in standing), and the sensations of dragging and fullness, as if the parts would fall. This is due to the distention and varicosity of the vaginal and uterine veins, caused by the formation of a proctoceles, pressing the vagina forward. Efforts in defecation then cause intense pain, pressing the vagina and rectum downward to the pubis and perineum; instead of relieving the patient, however, the traction on the vagina forces the uterus downward, and prolapsus or retroversion results. In this condition, the correction of the retroversion does not relieve the patient, since the cause is not the retroversion, but the rectocele, due to the constipation. The proper course to pursue is to cure the constipation, when the reposition of the uterus will cure the symptoms.

The view that the constipation and headaches frequently complained of by women with gynecological derangements are due to the latter is erroneous; the chief cause is to be sought in displacement or ptoses of the abdominal and pelvic organs. The writer has observed so many cases in which these symptoms persisted after all gynecological indications had been met that he feels that the work of Glénard fairly supplies the missing link in the etiological evidence. The usual displacement is a general descent of the bowels by which the cecum finds its way low into the pelvis, lowering the transverse colon and hepatic flexure, with obstructive angulation at the latter and at the splenic flexure. These displacements are not always accompanied by the uncomfortable symptoms; in some cases they may exist with a fair degree of health, but their diagnostic importance has been frequently confirmed by surgical ex-

plorations and the results obtained. C. A. L. Reed (*Jour. Amer. Med. Assoc.*, Aug. 3, 1912).

Constipation not caused by mechanical obstruction may result from impairment or suspension of the natural peristaltic motion of the intestines, and from paralysis of the nerves of the rectum concerned in the act of defecation, from irregular contractions of the circular fibers of the muscular coat by which regular peristalsis is prevented, from the reversing influence of continuous nausea, from excessive obesity coupled with loss of tone in the abdominal muscles, and from deficient mucous and glandular secretions, by which the feces are permitted to become dry and hard. In all these cases a careful manual examination of the abdomen will detect the presence of fecal accumulations in different parts of the colon and rectum. And their location will vary from day to day, instead of uniformly appearing in the same place, as in cases of obstruction.

Atony and spasm, one or both of them, are the principal causes of constipation and these may result from various morbid conditions. Atony generally predominates, but the spasmodic element, which often complicates, may be the chief factor. It may then show itself by the stools, appearing in a contracted form. A regular occurrence of greatly contracted stools should awaken the suspicion of an organic stricture. Boardman Reed (*Amer. Jour. of Gastroenterology*, Jan., 1912).

Chronic constipation is not accompanied by pains unless the colon is involved, and predominantly the ascending colon. The pains are restricted to the right iliac fossa, and are often ascribed to chronic appendicitis. Of his 32 patients with this "ascending constipation" the appendix had been removed on account of

persistent pains in 7. In his total series of 112 patients with chronic habitual constipation, appendectomy had been done in 11 cases and without improvement in a single instance. When the descending colon is involved, there is usually tenderness in the left side. The pains assumed the character of colic pains only in 6 of his total 112 cases. In these 6 cases of spastic rectum constipation the different parts of the colon were involved in about the same proportions. The writer agrees with Pinkus that the disturbances from habitual constipation are often erroneously ascribed to gynecologic lesions.

Again, he found that in healthy subjects the accumulating feces could stay in it for 8 hours during the day and 15 hours including the night without inducing a desire for defecation. This suggests that the reflex inducing defecation is not started by contact of the rectal mucosa with fecal matters, as some believe. In pure constipation in the ascending colon, pains were pronounced in 19 of 23 cases. In none of his cases of rectum constipation did he ever find the rectal sphincter abnormally contracted, not even in his 6 cases of spastic rectum constipation, but he noted an unmistakable spasm of the sphincter in 3 nervous patients with no tendency to constipation. Sphincter spasm can generally be traced to an anal fistula or hemorrhoidal tumor. T. E. H. Thaysen (*Ugeskr. f. Laeger*, Aug. 30, 1917).

**ETIOLOGY.**—Habitual constipation is more frequent in adults than in children, and more frequent in females than in males. Probably the most efficient causes of this condition are sedentary indoor habits with deficient outdoor muscular exercise. The first necessarily lessens the efficiency of respiration and internal distribution of oxygen, thereby lessening the tone and activity of the nervous and muscular structures generally,

and the omission of the latter still further lessens tissue metabolism and excretory processes. If we add to the foregoing the depression of the transverse colon and the crowding of the abdominal and pelvic viscera down upon the rectum by well-known female habits of dress, we will have the chief causes why females suffer much more from constipation than the male sex.

Ewald holds that there is, beyond doubt, a form of habitual constipation in which there is either diminished irritability of the intestinal nerves or defective development in the muscular coat of the intestine; an hereditary factor is often present. It may be acquired through habit of suppressing the desire, insufficient diet, or abundant diet difficult to digest, deficient in water, or too easily absorbed. Sedentary habits are also a cause, but obstinate habitual constipation may occur even in those who lead an active life. Disturbances in the circulation—as in heart disease, mechanical pressure, and particularly pregnancy—may produce it; but displacement of the bowel, such as occurs in Glénard's disease, is of doubtful influence. Adhesion of coils of intestine together, or to some other organ, is an occasional cause.

Rectal constipation may be, but is rarely, due to a nervous condition—*i.e.*, nervous rectum. While it may occur as the result of inflammatory conditions, such as hemorrhoids, fistulæ, and fissures, which are common to men and women alike, in very many cases it is occasioned because of the peculiar anatomical construction of the parts, and is mechanical in its origin. Anteversions, retrodisplacements, neoplasms (especially fibroids), and periuterine inflammations obstruct the downward passage

of the feces. Conversely, owing to the close juxtaposition of the rectum and the genital organs of the woman, a loaded rectum in its turn may occasion ovarian and uterine displacements and disorders.

A form of rectal constipation which heretofore has received but little recognition is that which occasions and is the result of the pulling down of the rectovaginal septum, thereby forming a pouch, constantly increasing in size, changing the direction of the intra-abdominal rectal pressure to that of the vaginal, which is at right angles to it, and making it difficult for the rectal sphincters to relax so as to void the contents of the bowel. The result is not only to render defecation difficult, but incomplete. The retention of fecal matter causes rectal irritation and autointoxication. This condition occurs not only in women who have borne children, but in nulliparæ and, though not so frequently, in the unmarried. G. P. Murray (*Medical Record*, Aug. 6, 1904).

A roentgenological study of spastic constipation showed in the great majority of the cases a marked degree of hypertonicity in the distal portion of the colon. Contrasted with this, the proximal portion of the large bowel exhibits normal tonicity with hypermotility. The line of separation between these two portions is variable in location, but is always found somewhere between the hepatic flexure and the end of the descending colon. G. Singer and G. Holzknecht (*Münch. med. Woch.*, Bd. lviii, S. 2537, 1911).

Another very common cause of constipation is the failure to adopt and persistently maintain a regular time for daily defecation. Many persons resist a desire to evacuate at the regular time from pressure of other engagements, and thus the nerves of the rectum become habituated to the contact of feces and cease to renew the desire to evacuate except at long intervals.

Dilatation of the colon is now classed among the important causes of constipation both in young children and in adults. This applies also to the first part of the colon, the cecum, and is often the cause of discomfort in the region of vermiform appendix.

In chronic constipation the cecum is progressively distended and forced downward and inward into the true pelvis. This results chiefly from its weight. This forcing down of the cecum is much helped by the sedentary position assumed during defecation. The squatting attitude is the correct one, as the pressure exerted by the thighs forces the cecum and transverse colon up into the abdomen. The inflammation of the colon and cecum consequent upon their excessive distention produces an adhesive process between the bowel and the peritoneum. The bowel thus becomes fixed, and it is less able to perform its normal functions and its muscle wall wastes. In many of these cases the kidneys are mobile. One of the most conspicuous of the clinical symptoms, besides the constipation, is a fullness and tenderness in the region of the cecum.

The symptoms due to the absorption of toxins all tend to produce an appearance in the patient of premature senility, and the loss of fat is very conspicuous. Mental depression is often present to a marked degree. As regards surgical treatment the choice lies between the division of bands and adhesions and the establishment of direct continuity between the lower end of the ileum and the termination of the large bowel. In women it is better to proceed at once to the deflection of the fecal contents from the greater part of the large bowel. Lane (*Brit. Med. Jour.*, April 1, 1905).

Crouching is the normal attitude and will often produce results when the common but ineffective sitting posture will not. Sawyer (*Lancet*, Sept. 16, 1911).

Surgical constipation implies any obstruction, dynamic or adynamic, of the terminal small or large gut in which surgical intervention is indicated. Lane and his school are the mechanists, while Keith, Alvarez, and the writer believe ' to be due to physiological impairment of the neuromusculature. The writer's "advancement" operation consists in removing the amount of large intestine advisable still retaining, however, the ileocecal valve and a small cuff of cecal wall containing the important nodal tissue; the anastomosis being between this cuff and the cut end of the retained large bowel. Care must be exercised that the ends of the ileocecal vessels are caught and ligated only as they appear in the cecal collar, not in the mesentery. W. H. Barber (*Interstate Med. Jour.*, xxiv, 9, 1917).

More or less distention of the colon is a common symptom resulting from accumulation of gases in nearly all the cases of ordinary constipation.

Atony of the intestine is a frequent cause of chronic constipation. According to Friedenwald, it usually affects the colon, which is unable to expel the feces. It may be primary, as the result of improper diet, sedentary habits, or a too frequent use of cathartics; or it may be secondary to many disorders, as obesity, disease of the heart, lungs; or liver, typhoid fever and other intestinal diseases, or organic nervous diseases. It is often found in childhood and may be congenital. The symptoms are marked constipation, headache, vertigo, nausea, and pains in the back and loins. Nervous symptoms are often present. The signs are marked tympany and sometimes the ability to detect the distended colon and fecal masses by palpation.

Dilatation as a primary patholog-

ical condition causing constipation, without having been preceded by either intestinal paralysis or some form of obstruction, is certainly of rare occurrence, as shown by Mr. Frederick Treves, who suggests "that the cases of idiopathic dilatation of the colon in young children are due to congenital defects in the terminal part of the bowel," and consequent obstruction.

In children obstruction from modification of the contents of the intestines and from defective action of the expelling muscular fibers or nerve plexuses innervating the intestine are the three main causes of constipation. Constipation in the mother, especially from lack of outdoor exercise, is a frequent factor in the constipation of infants. Congenital stenosis of the rectum may escape discovery for several weeks or months. E. Périer and Ganjoux (*Annales de méd. et chir. infantiles*, Oct. 1, 1911).

Constipation has been divided into several classes, based upon the pathogenesis of the various forms. The simplest and most satisfactory classification in respect to the treatment of the condition is probably that of H. A. Brav, which is in accord with the data submitted in the foregoing pages, and is as follows:—

1. *Mechanical Obstruction*.—Anything which prevents the passage of feces along the intestinal tract, such as strictures, hypertrophied sphincter or levator ani muscles, polypus, tumors, prolapsed or retroverted uterus, and enlarged prostate.

Many cases of habitual constipation are due to congenital and inflammatory bands, which draw the sigmoid into a sharp angulation near the left internal abdominal ring. The writer advises the systematic inspection of the site of this deformity, and the division of congenital folds and

inflammatory strictures. In addition to habitual constipation, will often be found associated such states as melancholia, neurasthenia, and hysteria, which are promptly relieved by the operation. J. R. Eastman (*N. Y. Med. Jour.*, June 24, 1916).

2. *Defective Peristaltic Action*.—This is chiefly due to lack of attention to the bowels. If the call of nature is not heeded, the feces may remain in the rectum, or they may be returned to the sigmoid flexure by reverse peristalsis. If the call of nature is frequently neglected, the mucous membrane loses its sensitiveness, and fecal matter accumulates in the sigmoid or rectum without causing any desire to defecate. Irregular living, coarse diet, and lack of fluid, are also apt to check peristaltic action.

3. *Deficient Intestinal Secretion*.—In this class the amount of bile emptied into the intestine is diminished.

4. *Deficiency of Liquid*.—This occurs whether due to a dry diet or to profuse sweating.

5. *Deficient Nervous Excitability*.—Organic disease of the brain or cord, neurasthenia, hysteria, old age, and lack of exercise, owing to weakness of nerve impulses.

6. *Muscular Spasm in the Lower Part of the Rectum*.—This is usually due to a painful fissure of the anus and ulceration of the rectal mucous membrane.

7. *General Disturbances*.—Lead poisoning, acute fevers, weakness of the abdominal muscles.

**PATHOLOGY**.—The various pathological conditions accompanying constipation have been sufficiently stated in connection with its diag-



nosis and etiology. Constipation, when permitted to continue several days, may give rise to irritation or inflammation of the mucous membrane in contact with the retained feces, causing temporary diarrhea with pain or tenesmus, and, though rarely, to perforation, peritonitis, and even death.

But the more frequent result is the formation of septic materials and their absorption, constituting a degree of autoinfection by which the general feelings of depression, loss of appetite, vertigo, and paroxysms of sick headache are produced.

Jules Simon rightly emphasized the indolence of the cecum occurring in children of sufficient age to be left considerably to themselves. They eat in a careless manner, and frequently eat too much. The food remains in the cecum and large intestine, giving rise to such symptoms as headache, incapacity for study, paleness, and irregular and capricious appetite. Deficiency of biliary secretion is an important cause.

Deficiency of biliary secretion is responsible for both constipation and the mucomembranous form of enterocolitis. Experiments were performed demonstrating the excitomotor and anticoagulant properties of bile. A stable, colloidal bile extract was prepared and administered in a large series of cases with good results. The diet should be such as will lead to a minimum of putrefaction and furnish a soft, easily eliminated residue. The first condition is satisfied by exclusion of readily putrescible albumins, such as egg albumin, and by limitation of fats. The second indication is met by the use of foods rich in cellulose. Nepper (*Monthly Cyclo. and Med. Bull.*, Jan., 1912).

**PROGNOSIS.**—When constipation is the result of any form of intestinal

obstruction the prospect of permanent relief will depend entirely on the nature and curability of the obstruction itself. But when it depends upon the loss of peristaltic action induced by erroneous habits of life, the prognosis is very favorable, provided the erroneous habits of the patient can be permanently corrected. All such cases can be temporarily relieved by suitable diet, laxatives, and tonic. Relapse, however, will soon follow unless all the primary causes are persistently avoided.

**TREATMENT.**—In the treatment of all cases of constipation the use of active cathartics should be avoided as far as possible. They tend to produce atonic paralysis of the intestinal musculature, thus creating a vicious circle.

In keeping with Bassler, the writer emphasizes the importance of defects of the lower colon in the production of constipation. Most cases are unquestionably injured by the daily use of purgatives and enemas. Many are due to toxemias engendered by obstructions which prevent propulsion of the intestinal contents all along the line, and cause the biochemical changes which in turn produce the symptoms usually termed autointoxication. Soper (*Southern Med. Jour.*, Feb., 1921).

Purgatives excite increased secretion to soften the fecal contents, and excessive peristalsis by which the intestine is evacuated, but leave the natural functions of the intestines more exhausted than before. Consequently, while they afford temporary relief, they never effect a permanent cure. To secure the latter, the actual causes of the constipation must be ascertained and removed.

Sedentary habits should be abandoned; the effects of indoor occupa-

tions counteracted by special open-air exercises mornings and evenings, sufficient to secure full oxygenation and decarbonization of the blood; eating freely of fruit, vegetables, and coarse or brown bread; avoiding all use of alcoholic drinks both fermented and distilled, and instead drinking a glass of natural laxative mineral water each morning, and persistently making an effort to evacuate the bowels directly after breakfast each day.

The following saline laxative is especially recommended in cases of constipation associated with hyperchlorhydria:—

℞ *Sodium chloride*. gr. xv (1 Gm.).  
*Sodium phosphate*. ℥ij (2.6 Gm.).  
*Sodium sulphate*. gr. xlv (3 Gm.).  
*Water* ..... Oij (60.0 c.c.).

Ft. solutio. Sig.: Take three or four wineglassfuls on rising, at intervals of twenty minutes. Hayem (*Quinzaine therap.*, Oct. 10, 1910).

In hepatic congestion complicated with constipation, the writers give every morning ten days each month, in a warm drink, 2 teaspoonfuls of

℞ *Sodium sulphate*,  
*Sodium citrate*,  
*Sodium bicarbonate* ..... āā 3 Gm. (45 grs.).

Huchard and Fiessinger (*Paris médical*, June 10, 1911).

The writer emphasizes the importance of proper diet in persons of sedentary habit: 1. Regular eating and not eating between meals. The full meal starts up a better peristalsis and exercises the musculature of the digestive tract. 2. Proper mastication of food. Bolting a meal means undigested food with fermentation and accumulation. 3. Eating the proper amount of food, not stuffing, but sufficient quantity, to leave sufficient waste to form bulk for the intestine to work upon. 4. The proper kind of food. The modern diet is too refined. Reversion to the

coarser foods is helpful. Also avoidance of too much coffee and especially tea. If the liver is sluggish it is well to limit considerably tea, coffee, sweets, fats, and pasty foods such as bananas and warm bread, etc., and increase the intake of cereals, juicy fruits, and vegetables leaving a large amount of residue, such as string beans, cabbage, cauliflower, turnips, spinach, kale, celery, etc., thus helping the bowel to work. Apples are especially good in some cases. The cathartic is gradually reduced as the bowel is found to act of itself, and is finally omitted altogether.

Theoretically, **organotherapy** would seem ideal by restoring the normal secretions of the gastrointestinal tract in treating constipation, but the mechanical factor cannot be eliminated altogether and to the exercise may well be added **massage**. W. M. Gardner (*N. Y. Med. Jour.*, Mar. 18, 1916).

A valuable addition to our harmless means is the use of olive oil. From 3 to 4 ounces (90 to 120 c.c.) injected at night are readily retained and insure a copious passage next morning.

The use of irrigations of sterile olive oil is recommended by the writer in the treatment of constipation. A fountain syringe is employed, to which a soft-rubber catheter, which is passed about three inches into the rectum, is fitted. The oil is introduced about two hours after the evening meal, the patient lying on his back or left side. The quantity given is from about 2 to 7 ounces (60 to 210 c.c.), and its temperature should be about 95° F. (36.1 C.). After the tube is inserted the reservoir of the syringe is elevated to about three feet above the patient and the oil is allowed to flow slowly into the rectum. Should there be difficulty in inserting the tube, the rectum should be cleared by means of an irrigation of saline solution. The oil should be retained all night, and in the morning, on rising, an irrigation of about a pint of saline solution at 100.5° F.

(38° C.) is taken. This should be retained for a few minutes. The oil injections are given daily at first, but after a week the intervals may be lengthened until one every five days becomes sufficient. Vidal (*Jour. de méd. de Paris*, xx, No. 2, 1908).

**Glycerin** is another mild, though active agent. It may be administered in the form of suppositories available in the shops or be injected directly into the rectum.

Among the mild, but efficient agents is **agar-agar**, which is thought to act mechanically when coarsely comminuted and mixed with food. It is transformed into a jelly in the stomach, and, being unabsorbable, gives greater bulk to the feces. The dose ranges from 1½ drams (6 Gm.) to ½ ounce (15 Gm.).

The constant or daily use of **agar-agar** brings about normal evacuations. It is helpful and harmless; may be used indefinitely without impairing the effects of drug treatment. Gompertz (*Practitioner*, May, 1910).

The writer recommends **phenolphthalein-agar**, containing 0.03 Gm. (½ grain) of phenolphthalein in 1 Gm. (15 grains) of agar, and **rhubarb-agar**, containing 1 c.c. (16 minims) of fluidextractum rhei in 1 Gm. (15 grains) of agar, prepared by dissolving the remedy in boiling agar water solution, thoroughly mixing, evaporating to the original dry agar volume, and grinding up into flakes. The dose is 1 teaspoonful twice daily in water after meals. Einhorn (*N. Y. Med. Jour.*, May 30, 1914).

The writer has prescribed rather more than 1000 doses of **phenolphthalein**. The dose for children is ½ to ¾ of a grain (0.03 to 0.048 Gm.), and for adults 2 to 6 grains (0.13 to 0.4 Gm.). He has given it usually in doses of about 1½ grains (0.1 Gm.) repeated from 2 to 3 times a day; it produces loose motions in from 4 to 6 hours after a dose of 3 to 4 grains (0.2 to 0.26 Gm.), but

where smaller doses are given it brings on a natural or somewhat soft and copious evacuation only once or twice daily. It is singularly painless as a rule. It does not seem to lose its effect for a considerable time. McWalter (*Lancet*, Nov. 20, 1915).

To aid in restoring intestinal peristalsis a pill or capsule may be given each night containing ⅓ grain (0.021 Gm.) of extract of **nux vomica** and 1 grain (0.065 Gm.) each of extracts of **cascara sagrada** and of **hyoscyamus**. If no evacuation takes place the following morning an **enema** of warm water may be used after breakfast.

An effective tablet recommended by Boynton is composed of **nux vomica** extract, **podophyllin resin**, **belladonna** extract, and **aloin**, ⅓ grain (0.006 Gm.) of each, and is excellent for the average cases of longstanding constipation. The tablets should be taken before or after each meal, and, if the effect is too active, half a tablet, more or less, may be given at each meal.

**Beech creosote** is regarded as one of the best remedies for habitual constipation. It should be given pure, twice daily during or after meals, in doses of 1 to 8 drops (0.06 to 0.5 c.c.), beginning with the smaller and increasing until the desired effect is secured; the vehicle is always water, wine and water, or milk.

In some cases of special atony of the sigmoid flexure of the colon and rectum **aloin** or extract of **colocynth** may be used with advantage instead of the **cascara sagrada** in the pill.

An important factor in the production of intestinal atony is a deficiency of bile. The preparations of **ox-bile** available may be used advantageously either alone or in conjunction with other hepatic stimulants.

The writer uses the following pill in the treatment of chronic atonic constipation:—

R *Purified ox bile*.. gr. j (0.06 Gm.).

*Extract of colocynth,*

*Extract of hyoscyamus,*

*Extract of nuxvomica* .....ãã gr. ij (0.13 Gm.).

M. et ft. pil. no. j.

Sig.: One pill at bedtime.

Gant (N. Y. Med. Jour., March 26, 1910).

Mucomembranous enterocolitis and constipation being the result of insufficiency of the biliary secretion, their treatment becomes simple. The general indications are: (1) reduction to a minimum of the quantity of toxic and putrefactive products in the intestine by an appropriate diet; (2) shortening of the period of transit of food through the alimentary canal and prevention of the coagulation of mucus by the use of a cholagogue, the best of which is **bile** itself. The writer uses an extract devoid of putrescible nucleoalbumins, available in 0.20-Gm. (3.1 gr.) dragées; suppositories, and ampoules of 50 c.c. (1.7 fluidounces) in which the biliary substances, dissolved in water, occur in the concentration of normal bile. H. Nepper (Monthly Cyclo. and Med. Bull., Jan., 1912).

The troublesome constipation met with in infants can best be overcome generally by giving them **fresh air**, **proper food**, and a rectal **enema** of warm water containing a little **chloride of sodium** at a stated time each day, without any medicine by the mouth.

When there is alternately diarrhea and constipation in infants the cause, according to Lawrence, is usually an excess of proteids. **Essence of pepsin**, 10 or 15 drops (0.6 to 0.9 c.c.), should be given after nursing, and **abdominal massage** is of value. An excellent

plan to secure an action of the bowel at a regular time is the insertion of an **oil-paper suppository**. The constipation of bottle-fed infants being commonly the result of a deficiency of fat in their food, the rational treatment embraces the addition of **cream** and **butter**. All forms of teas should be strictly prohibited, and in older children too much potato should not be allowed.

In artificially fed infants constipation may, on the one hand, according to Blackader, be due to an insufficiency in the fats or proteids. The addition of a teaspoonful of fresh **cream** for each teaspoonful of condensed milk used is an effective way of relieving the constipation following feedings of condensed milk. **Beef juice** is occasionally laxative. When constipation is due to congenital stricture of the anus or rectum, rectal examination will reveal the seat of the difficulty. When nutrition is defective, **malt extracts** and **codliver oil** may be tried. **Enemata** should be employed for a comparatively short period only, and **saline solution** is recommended.

In infantile constipation Dorfler found that excellent results could be obtained from administration of fresh **butter**. A half-teaspoonful is given to children of from 1 to 3 months, with a spoonful of coffee morning, noon, and night. Children of from 5 to 12 months are fed with from 1 to 3 teaspoonfuls of butter at evening, every two or three days, this being continued until the stools are regulated. When a normal condition of the bowels is reached the remedy should be discontinued and resorted to again if the trouble recurs. Absolutely fresh, saltless butter should be

employed. The butter seems also to improve nutrition.

Congenital deficiency of the muscle sense of the rectum is not uncommon in infants, and, occasionally, lasts through life. It should always be suspected in severe cases of constipation in infants and children when ordinary methods of treatment by diet, aperients, and abdominal massage have failed. It soon leads to secondary retention of feces in the pelvic colon; the irritation caused is likely to give rise to colitis. Aperients are useless. If defecation is difficult and painful liquid **paraffin** is given and the child required to sit at stool for at least ten minutes after breakfast. If this fails, **water** or a **glycerin enema** is given and the attempt repeated. Glycerin is most effective: 1 ounce (30 c.c.) the first day; next day 0.5 dram (2 c.c.) of the glycerin is replaced by water; third day 1 dram (4 c.c.), etc., until all is replaced by water. The amount used is reduced by one-twentieth part at a time until no more is required. In all cases in children a cure eventually results, but if allowed to continue until adult life it may be necessary to use enemata permanently. If the injection is given under low pressure, and the glycerin is as dilute as possible, and as little water as possible, the enemata never lose their effect. Hertz (Brit. Jour. of Children's Dis., April, 1912).

In the rare cases in which a fair trial of enemas and suppositories does not succeed a few drops of the elixir of **cascara sagrada** may be given each evening.

**Massage** is gradually affirming its value. In conclusions based upon study of 147 cases, le Marmel showed (1) that mechanical treatment can be classed among those therapeutic agents whose action on the circulation, respiration, and general nutrition is decidedly energetic; (2) that it modifies the abdominal circulation

and dispels certain passive congestions, especially those of abdominal plethora; (3) that it increases the muscles in volume and strength; (4) that it is the best curative agent for constipation from muscular paresis or paralysis not due to central nervous disease; (5) that it is the best curative agent for constipation dependent on hypoaesthesia or anesthesia due to local causes; and (6) finally, that it is formally contraindicated when the constipation is due to acute inflammation or to tumors.

The following process of **massage** for constipation is far more efficient, according to Kummerling, than the usual process. The patient is placed on his right side and the operator picks up with his thumb and index of each hand the skin and the subcutaneous tissue at the level of the iliac spine. This makes the intestine directly accessible to the other fingers, and he manipulates it with them, always pressing from above downward, and with the ends of his fingers, for five minutes. Then the patient is turned on the left side and the process is repeated on the cecum and the ascending colon, only in the opposite direction, from below upward. This leaves only the small intestine and the transverse colon to be massaged, for which the patient is placed in the decubitus genupectoral position, as this relaxes the abdominal walls and brings the intestines closer into the hand of the operator.

To perform **abdominal massage** on infants, J. Madison Taylor recommends the following technique: The mother anoints her hand with sweet oil or vaselin and slowly and carefully kneads the abdominal walls, grasping the superficial structures and rubbing

them upon the underlying ones, following, respectively, the course of the ascending, transverse, and descending colons, and ending with a circular movement of the hand around the umbilicus.

There is a class of cases in children in which any and all forms of treatment result merely in improvement, but not in permanent cure. **Massage, oil enemas, and hydrotherapy** should be used simultaneously. The indiscriminate use of antispasmodics and soothing laxatives is to be deprecated. The following remedies are harmless and often efficient: **soap and glycerin suppositories, cacao-butter suppositories with aloin, belladonna and tincture of nux vomica, calcined magnesia, magnesia and rhubarb, compound licorice powder, castor oil, cascara sagrada, calomel** followed by a **saline aperient**, and the standard **mineral salts, or waters**. Whatever the form of therapy, a habit of regular stools should be established. Sheffield (*Archives of Pediatrics*, Nov., 1905).

Constipation is rare among children of the East. Their regular habits of defecation are inculcated from the birth of the child. When the child awakes in the morning the mother takes the buttocks of the infant between her two hands and holds the child up with its back toward her, pressing its thighs against the abdomen and supporting its back with her thumbs and knees. The infant is thus induced to strain on account of the position, and coaxed to do so by the mother. Budberg (*Therap. der Gegenwart*, July, 1910).

In the chronic constipation of infants, **liquid paraffin** in large doses gave the writer the best results he had obtained. With it and **lactic acid bacilli** very remarkable results may be obtained in diseases caused by putrefactive or allied poisons absorbed from the intestines. Hill (*Arch. of Pediat.*, Feb., 1915).

The writer found physical measures the most useful of all in constipation,

especially **warming compresses** over the whole abdomen at bedtime. A cold compress is first applied, then a piece of some impervious material, next a layer of cotton wool, and finally a flannel bandage. This compress is to be kept on the whole night unless the patient wakes some hours after going to sleep, in which event it may be removed at that time. When the compress is removed it is found in a steaming condition; it is the transition from coolness of the abdomen to the heated condition which awakens the motility of the intestinal involuntary muscle. **Massage** of the abdomen, by the patient himself or by another person, the strokes being executed circularly for about 5 minutes morning and evening, is also a valuable measure. The masseur's hand should be covered with petrolatum or talcum powder. P. Merklen (*Bull. méd.*, Apr. 1, 1914).

In the habitual constipation of infants the writer emphasizes the need for differentiating the cause in order to apply proper treatment. In the constipation connected with atony, all measures to stimulate the organism should be applied, including general **salt baths** followed by **rubbing with alcohol** and **massage** of the abdomen. When the atony seems to be due to weakness of the reflexes, and this is traceable to anesthesia of the mucosa, immediate and often remarkable results can be obtained by introducing into the rectum a **blunt tipped cannula** or glass stirring rod. This is left in contact with the mucosa for a few minutes, moving it around a very little. The mere presence of this foreign body, its light rubbing of the mucosa, usually entail an evacuating reflex. This simple procedure can be tried in all forms of constipation.

The passage of hard feces causes erosion of the mucosa of the anus, and the pain from this causes the child to repress desires to defecate, or may induce spasm of the sphincter. Laxatives do not cure constipation

and may aggravate it. Yet, Marfan's choice, **sodium citrate**, can be given up to 1.5 to 2 Gm. (22 to 30 grains) a day without harm. Calomel should never be used in infants; the writer has known it to bring on severe acute dysenteriform enterocolitis. When the result of hypertonus or spasm, **belladonna** may be indicated. The writer pulverized 0.004 Gm. ( $\frac{1}{40}$  grain) per year of age, with some mild laxative. Dorlencourt (Le Nourrisson, Jan. 1918).

Never give castor oil unless there is diarrhea. A child should gain from 4 to 7 ounces per week. Underfeeding is evidenced by a small and insufficient stool. It is better to give small quantities of milk after each feed than to replace 1 or 2 feeds by a bottle-feed, as the natural stimulus of sucking is thus not interfered with. Insufficient fat is liable to produce constipation; on the other hand, too much fat is to be avoided, and if the stools become pasty and greasy the quantity should be reduced. In case of faulty fat digestion some **pancreatic extract** should be given. Curds in the stool should be examined to see if they consist of undigested milk or small rolls of dried mucus; if the former, **humanized** or **citrated milk**, should be given, and in case of the latter, **liquid paraffin** is indicated. If the stools are too dry the feed should be further lubricated or the child given **sips of water between feeds**, the water always being first boiled. Too much water must also be avoided, since the bowel becomes lazy if stools are always watery. A little fruit juice each day is of benefit. After an attack of acute diarrhea, the tone of the bowel must be restored and if simple hygienic measures do not suffice, a mixture of **cascara**, **nux vomica**, and **liquid paraffin** may be given. Mothers should be warned of the danger of the indiscriminate use of soap suppositories as if this remedy is resorted to too frequently the natural stimulus of rectal reflex is lost. V. Borland (Lancet, Mar. 22, 1919).

**Vibratory massage** practised with one of the numerous instruments now available is of distinct value in cases in which chronic constipation is due to intestinal atony.

**Electricity and hypnotic suggestion** have also been recommended. The first may be classed as an adjuvant to massage of no mean value in cases of intestinal atony, while the second may be considered as meriting but little confidence.

An agent was obtained by Zuelzer, Dohrn, and Marxer, in 1908, from the gastric mucosa, which was found to enhance peristalsis very actively; but this organ giving very small quantities of this agent, further research showed that it could be obtained in relatively large quantities in the spleen. A preparation known as **hormonal** is said, injected intravenously in doses of 5 drams (20 c.c.), to give very active results in intestinal paralysis following operations and volvulus, but its use has given rise to dangerous symptoms in so many instances that it is being abandoned.

Series of 6 cases of grave intestinal paralysis which had resisted all other means. **Hormone** injections caused general improvement and the emission of gas in from one to five hours after the injection. But the effect did not seem to be lasting. It is advisable to enhance the action by means of enemata and purgatives to insure the elimination of the intestinal contents. Heule (50th German Congress of Surg., April, 1911).

Results from the use of **peristaltic hormone** in 26 cases of constipation. There was some degree of improvement in about 50 per cent. of the cases treated. The duration of the favorable effects was very variable, but in general quite brief. The longest time that the good effects lasted was four months and one

week. *Lincoln (N. Y. State Jour. of Med., March, 1912).*

**Petrolatum** is an efficient agent and is being increasingly employed. It lubricates the canal while softening the stool, thus avoiding all irritation.

A vegetable oil cannot serve as a lubricant for the feces, until the amount ingested surpasses the dose normally saponified by the liver and pancreas. Hence, to take olive oil for the purpose, as some recommend, imposes a useless burden on these 2 organs. **Liquid petrolatum**, on the other hand, seems to traverse the alimentary canal without exciting any reflex action in the liver. Three years of experience with refined liquid petrolatum have confirmed its valuable lubricating action and its healing influence on the minute excoriations from hard feces. *Le Tanneur (Paris méd., June 24, 1916).*

**Bran** has been highly recommended by A. E. Gallant (*New York Medical Journal, August 31, 1912*). It acts mainly by exciting peristaltic action reflexly. One to two heaping table-spoonfuls in a glassful of cold water, taken on retiring, act next morning. In some it may be necessary to take a **cascara sagrada** laxative a few days until the habitual stool is established.

Patients with habitual constipation often get used to laxative drugs. The writer found **bran** successful in cases where every other means had failed. The autointoxication due to the accumulation of feces in the bowel is prevented when active peristalsis is insured, and the intestinal contents kept moving. Bran has proved a most serviceable agent for this purpose. *A. E. Gallant (N. Y. Med. Jour., Jan. 18, 1913).*

There can be no doubt as to the value of **bran** in constipation. There are, however, certain cases in which, although there is no anatomical condition causing obstruction, bran fails altogether. In such instances, al-

though the writer gave the patient daily an ounce and a half of bran and an ounce of **agar-agar**, besides **prunes**, **exercise**, **water**, etc., the bowels, after acting well perhaps for a few days, then slowed up, and it became necessary to supplement this hygienic treatment with **cascara** or some similar agent. Still, in a large number of cases bran proved all that was required. It is certainly a most valuable agent. *Anthony Bassler (N. Y. Med. Jour., Jan. 18, 1913).*

[The trouble with most cases of constipation as ordinarily seen is a loss of muscular power or peristalsis, or a deficiency of intestinal secretions, or, again, of both these factors acting jointly—causes which have been reviewed at length under *Etiology and Pathology*. If to these factors we add irregular habits, the vast majority of cases are accounted for. Next in the order of frequency is the indiscriminate use of purgatives which tend to induce intestinal atony.

As to treatment, the use of tonic laxatives administered as shown below, and with a view to producing a tonic laxative effect, is by far the best means of improving the form of constipation due to the above conditions. For this purpose I use the following combination:—

**R** *Fluidextract of cascara sagrada* (P. D. & Co.) ..... f℥iss (45 c.c.).  
*Glycerin* ..... f℥j (30 c.c.).  
*Essence of pepsin*  
 (Fairchild's),  
 q. s. ad ..... f℥vj (180 c.c.).

**M. Sig.:** One teaspoonful in water ten minutes before meals, regulated as needed for bowels.

Used in this manner a tonic laxative effect is obtained without producing gripping or purging. **JOHN A. WITHERSPOON.**]

Various **operative procedures** have been proposed. **Divulsion of the anus** has been advocated, but the after-effects, particularly if the fibers of the sphincter are ruptured, are not always such as to recommend the procedure.



According to various surgeons, constipation from invagination of the sigmoid and upper rectum into the ampulla occurs far more frequently than is generally supposed. It is noted chiefly in adults and in the female. This invagination may be due to an abnormally long sigmoid or an elongated mesentery, or to any condition which excites frequent or straining efforts at defecation. The earliest symptom is imperfect and unsatisfactory bowel movements which do not relieve the desire to defecate. As a result of prolonged irritation and catarrh, ulceration of the sigmoid and rectum is produced. Autointoxication is common. **Colopexy** is advocated as the shortest method to obtain a cure.

The writer does not believe that excision of the colon is either necessary or desirable in intractable constipation. Better results can be obtained by seeking the cause of the condition and remedying it directly when possible. Where this is not possible **appendicostomy** gives results which will compare very favorably with those of excision of the colon, and at the same time this is an operation with practically no mortality. Mummery (Lancet, July 20, 1912).

All cases of intestinal stasis, so called "abdominal neurasthenics," should first be carefully treated medically for a number of months, operation being resorted to only when this fails. In operating the writer either freed any bands found or did an **ileosigmoidostomy** or **cecosigmoidostomy**. Among the 75 patients on whom he had operated in the last 5 years 46 per cent. had been greatly improved, 32.5 per cent. improved, 12 per cent. unimproved, 5.5 per cent. had died, and 4 per cent. had not been heard from. These figures justified continuance of the operative procedures for intestinal stasis. J. Shelton Horsley (Trans.

Amer. Med. Assoc., N. Y. Med. Jour., July 7, 1917).

In a personal case the benefit from **ileosigmoidostomy** in the young woman was so pronounced that it certainly encourages further trials of this shortcircuiting method in treatment of habitual obstipation. The various other technics for remedying this condition are described with this, and its advantages extolled in cases of constipation for which no cause can be discovered and vagotomy or sympathectomy seems to be responsible. Ceballos (Rev. de la Asoc. Med. Argentina, Aug., 1917).

The possible existence of some exciting cause in women, especially when chronic constipation is associated with pain in the right iliac fossa, has often led to **removal of the appendix**. In most instances, however, lesions were found in neighboring structures, particularly in women, the constipation being due to obstruction caused by external pressure.

Having often seen apparently healthy appendices removed without benefit to the patient, the writer determined to open the abdomen by a median subumbilical incision in search for a possible cause. In all patients thus operated the inlet to the pelvic cavity was found considerably obstructed by the left broad ligament, the latter having assumed a horizontal instead of a vertical position, thus forming a distinct shelf. He also noted that the proximal portion of the pelvic colon rested on this shelf, and that the remainder of that portion of the bowel, in order to pass downward into the cavity of the pelvis, was obliged to cross over the tense free border of the ligament with the result that a definite kink in the lumen was made. This explained the obstruction to the fecal movement in the colon. Moreover, adhesions were found between the broad ligament or the uterine adnexa and the pelvic colon and were contributory to peristaltic impediment. This convinced

the writer that obliteration of the left broad ligament was the only means by which the obstruction to the pelvic inlet could be remedied, and he devised an operation by which it could be done.

The operation consists of removing a wedge-shaped piece out of the ligament, the base of the wedge being situated at the free border of the ligament.

The principal symptoms indicative of the obstructive effect of a proptosed left broad ligament on the passage of feces along the pelvic colon are (a) constipation; (b) left iliac pain; (c) right iliac pain; (d) flatulent distention of the abdomen; (e) gastric disturbances; (f) passage of mucus by rectum; (g) pain in the lumbosacral region; (h) a state of chronic invalidism. The writer operated on 150 patients with highly satisfactory results. With two exceptions they were all relieved. W. E. Miles (Chicago Med. Recorder, April, 1910).

Two cases reported in which the obstruction was from adhesions at the right angle of the colon.

Presence of constipation from obstruction at this point is peculiarly harmful, as the feces are kept in a semifluid condition by the constant arrival of intestinal juice from the small intestine. This permits absorption and consequent chronic intoxication, the results being much more serious than when the feces stagnate in the rectum or descending colon. When they reach this region they are dry and bacterial life is arrested. The bowel contains here merely hard, dry bodies without toxic action. In both cases no benefit was derived from medical measures, but conditions rapidly improved after laparotomy with separation of adhesions and resection of superfluous omentum in one case. Roux (Arch. des mal. de l'app. digestif, May, 1910).

Congenital conditions alone account for some chronic cases. Suspension and excision operations are

valuable, according to J. G. Clark, in certain cases, but disappointing in the remainder. At best these fixation points may be unstable. Radical excision of obstructive portions of the large bowel may give the highest percentage of operative mortality, but is likely to give the best ultimate results in the survivors. In no field of surgery are greater care and experience needed than in this.

The operations available include: (1) suspension of the sigmoid flexure; (2) suspension of the transverse colon (ventro-omental fixation); (3) excision of the sigmoid; (4) erosion of the sigmoid and suspension of the transverse colon; (5) lateral anastomosis from one limb of sigmoid to the other; (6) excision of the transverse colon.

Surgical intervention is also necessary in the presence of: (1) hypertrophied O'Beirne's sphincter, a band of muscular fibers located in the rectosigmoidal flexure; (2) hypertrophy of Houston's rectal valves, which occasionally follows chronic colitis, ulcerations, and other diseases of the lower bowel; (3) hypertrophy of the levatores ani muscles, which may thus form rigid bands capable of partially or completely blocking the passage; (4) hypertrophied sphincter muscles which do not yield to medical treatment; (5) inward deviation of the coccyx and pressure of this bone upon the rectum, causing obstruction, and, finally, (6) foreign bodies lodged in the rectum or beneath the mucosa. All these conditions are diagnosed mainly by the use of the proctoscope and digital examination.

JOHN A. WITHERSPOON,  
Nashville.

**CONSUMPTION.** See TUBERCULOSIS, ACUTE, AND CHRONIC PULMONARY.

**CONVALLARIA MAJALIS.**—

The lily of the valley, a native alike of Europe and North America, has long been held in high repute in Russia, Germany, and Scandinavia as a plant possessed of great therapeutic virtues, rivaling those of purple foxglove. It is a perennial; has a creeping, much-branched rhizome of about the thickness of a quill; two or three elliptical and smooth radical leaves; a one-sided raceme of ten or twelve light, nodding, bell-shaped, six-lobed, white flowers; very fragrant, but of acrid and bitter taste. As found in shops, it appears in cylindrical, wrinkled, whitish pieces marked by circular scars. Both the rhizome and the roots are medicinal.

The active principles are two glucosids, denominated, respectively, convallamarin and convallarin: the first a pale-whitish-brown, amorphous powder, soluble in both alcohol and water; the second a brownish-white powder, soluble in alcohol only.

**PREPARATIONS AND DOSES.**—

*Convallariæ radix*, N. F. (convallaria), 7½ grains (0.5 Gm.).

*Fluidextractum convallariæ radicis*, N. F. (fluidextract of convallaria), is given in the dose of about 8 minims (0.5 c.c.).

Unofficial are:—

*Convallamarin*, ¼ to 2 grains (0.016 to 0.13 Gm.).

*Convallarin*, 2 to 4 grains (0.13 to 0.26 Gm.).

**PHYSIOLOGICAL ACTION.**—Moderate doses slow and strengthen the heart's contractions; larger doses accelerate the heart and induce irregularity; toxic doses cause progressive paralysis, muscular tremors, complete loss of reflex action, and death when the heart is arrested in systole. Doses that slow the heart heighten arterial tension; the drug probably also acts directly upon the blood-vessels. Respiration is deepened and slowed by this drug, toxic doses causing the respiratory movements to become very slow and full. Like digitalis, it is a most efficient diuretic when given in the form of an infusion, but is apt to be uncertain in its effects upon the kidneys when exhibited in any other form; it is also emetic and cathartic. While the effect upon the circulation is very like that

of foxglove, it is a more uncertain remedy, and likewise a less powerful one.

While the tonic action on the heart is about the same with both convallamarin and lily of the valley, the diuretic properties are in great part to be attributed to the fresh convallarin. Unfortunately the drug varies considerably in strength, depending upon the quality of material employed, the use of heat in the manufacture of the extract, and other unknown factors. Hence a constant pharmaceutical preparation in the form of the juice of the fresh plant is necessary. It contains 2.25 Gm. (35 grains) of convallamarin and 1.2 Gm. (19 grains) of convallarin per kilogram (2¼ pounds), possesses all the physiological properties of the plant itself, and may be employed in doses of from 5 to 15 cg. (½ to 2½ grains), gradually increasing by 5 cg. (½ grain). D. Laigre (Rev. de théér. méd.-chir., Nov. 15, 1903).

Convallamarin reduces the pulse rate, markedly increases the flow of urine, and is "cumulative" in exactly the same way that digitalis is: i.e., when exhibited in a way that fails to provide for or secure proper elimination; because of this "cumulative" bugbear, it has been suggested that more than one dose during twenty-four hours should not be administered to the same patient; but this precaution is entirely superfluous if the drug is exhibited intelligently and its effects carefully watched. This glucosid, however, is in every way inferior to preparations of the entire drug, and all the latter are inferior to the infusion.

Convallarin is both emetic and purgative.

**THERAPEUTICS.**—Opinions differ greatly as to the value of the drug in dilatation of the heart and atony of its musculature—in all conditions, in fact, in which digitalis is used with advantage. It is especially useful in tobacco heart, a condition in which digitalis does not always act favorably.

The two symptoms connected with the weakened heart and "soft" pulse of tobacco excess, viz., a congested or dusky-red color of the skin of the nose, general cold to the touch, and also,

especially in winter, cold feet—conditions due to feeble circulation—the writer finds much benefited by the use of the fluidextract of *convallaria majalis*, which has not the cumulative action of *digitalis*. H. S. Purdon (Dublin Jour. of Med. Sci., Aug., 1900).

The writer has had very extensive and successful experience with *convallaria*. It has none of the disagreeable by-effects and after-effects of *digitalis*,—the cumulative character and the disturbance of the stomach,—being itself one of the best stomachic tonics available. It may be used to excellent advantage in **tobacco heart**, in the asthmatic breathing from enfeebled heart, and in **chronic asthma**. Lenneker (Therap. Gazette, Sept., 1907).

*Convallaria* has been lauded by some and by as many condemned. It should be remembered, however, that the strength of the different preparations of different manufacturers varies. Again, some employ the petals of the flowers only; some the rhizome; some the root; some the entire plant. Justice demands a standard be set, and the plant studied more carefully from such a definite standpoint.

In **dropsy** of renal or hepatic origin *convallaria majalis* in an infusion of 4 Gm. (1 dram) of the plant to 180 Gm. (6 ounces) of water, a tablespoonful every two hours, changing later to a 1:12 alcoholic tincture, of which 45 to 80 drops (2.8 to 5 c.c.) were taken during the day, was found very efficient by Jabowski, who also noted that it favorably influenced the renal function in **hepatic cirrhosis**. S.

## CONVULSIONS, PUERPERAL.

See PUERPERAL ECLAMPSIA.

## CONVULSIVE DISEASES OF INFANCY AND CHILDHOOD.

—Infants and children under 2 years of age are well known to be peculiarly liable to convulsions. The causes of this tendency are as yet subject to some confusion. Much light has been shed on the subject, of late years, by

a number of careful observers, among whom may be mentioned Soltmann, Escherich, Kassowitz, Baumé (1805), Féré, Tarchanoff, Lemoine, Paneth, Thiemich, Hochsinger, Huebner, Erb, Burkhardt, Kalescher, Gangenhöfer, Mann, Frankl-Hochwart, Trousseau, Chvostek, Schultze, Pfandner, and Sajous, and the physiological studies of Fritsch and Hitzig.

To the painstaking observations of Soltmann we are indebted for a clear clinical picture of the processes and phenomena involved. He learned from experimental investigations that in newborn dogs, cats, and rabbits the motor cortical areas discovered by Fritsch and Hitzig cannot be excited electrically and are probably incapable of functioning. He concluded that they are incapable of exercising either an innervating or an inhibiting influence on subcortical motor centers. The human infant was shown, by his comparative studies of medullary striation, to require twelve to eighteen months to attain the stage of development of an animal from ten to twelve days old. Thus it would seem that the inhibitory mechanism is not well developed and does not become effective before that period in the human being. This explains the frequency of convulsions in infants under eighteen months.

Irritability of the peripheral nerves was found also to have attained the maximum, or even to have exceeded it, at a more rapid rate than that of the inhibitory centers. Hence a trifling irritation will affect the infant before the development of the inhibitory mechanism more seriously than an older child, and vastly more than an adult (Thiemich).

The term "physiologic spasm-

philia," or an "increased disposition to reflex irritation," was used by Soltmann to describe the state of insecure neuronc balance. This gives us a useful descriptive phrase, but does not explain the causal factors, for which a host of plausible scientific theories are advanced by Kassowitz and others. As will be set forth under Infantile Convulsions, the explanation most in accord with clinical and pathological experience is that offered by Sajous—irritation of the spasmogenic nerve-elements by imperfectly catabolized and therefore toxic wastes.

In studying the phenomena of convulsive disorders there is no clinical method yet devised for measuring the mechanical irritability of a nerve; we must rely on electric excitation. This has been done by Erb in adults, and later by Burkhardt, Kalescher, Escherich, Gangenhöfer and Hauser, Mann, and Thiemich.

### INFANTILE CONVULSIONS (INFANTILE ECLAMPSIA).

Convulsions occurring in young children constitute a symptom, not a disease. They vary widely in severity, in proportion to (a) the spasmogenic susceptibility of the individual; (b) the dynamic potentiality of the exciting cause, and (c) the presence or absence of conditions favoring reflex irritability, endogenous or exogenous.

**SYMPTOMS.**—The clinical picture of the condition so closely resembles epilepsy that till recently (Féré, quoted by Thiemisch) infantile eclampsia was regarded as a form of epilepsy characterized by a favorable course. The attacks consist of a primary tonic and a secondary clonic stage. A kind of aura is also often observed, a rest-

lessness, distracted anxious expression lasting a few moments, followed by pallor, suspension of consciousness, and a tonic convulsion of the muscles of the eye, face, and extremities. After a few moments clonic convulsions occur, jumping, jerking, like muscles influenced by powerful electric currents; also cyanosis and sweating. After a time all this subsides, a general relaxation ensues, and consciousness returns. The somnolent stage of epilepsy does not occur.

In the differential diagnosis of convulsions, the writer states that when the patient suddenly sees things around as if removed to a distance or becomes very small, the trouble is more liable to be *hysteria* than epilepsy. An actual epileptic seizure must have occurred before it is possible to label the case as epilepsy. Night convulsions, waking out of sleep, are apt to be epileptic. Fainting may be the first manifestation of petit mal. Loss of consciousness seldom lasts longer than 30 minutes in epilepsy, while in hysteria prolonged unconsciousness is the rule. Flinging the arms around and curving the whole body (*arc de cercle*) speak for hysteria, but an epileptic may also have hysteric convulsions. Flatau (Med. Klinik, Jan. 7, 1917).

If the attack lasts longer than five minutes, the suspicion of real epilepsy is entertained. Duration is seldom more than a few moments. A series of paroxysms sometimes occur at short intervals, closely resembling status epilepticus. These may be at longer intervals and yet continue for several days. Death seldom results. Laryngospasm and expiratory apnea ("breath-holding") may prove fatal.

In a study of the calcium-magnesium-phosphorus balance in children subject to convulsive disorders in cases classified as epileptics of the

petit mal type, it was found that none of them gave a history of epilepsy in the family and that nearly every one of the children subject to convulsive attacks had a low balance in either magnesium, calcium, or phosphorus, though in none was the balance lowered in all 3 substances. By estimating the percentages of retention and absorption one can come very close to the actual state of mineral metabolism. In convulsive disorders of this type a search should be made for mineral deficiency, and if such a deficiency is found the attempt should be made to raise it to normal. Hoobler (Trans. Amer. Pediat. Soc.; Med. Rec., Sept. 4, 1920).

An examination of the eclamptic child during the intervals of freedom will enable one to differentiate between this and other functional or organic convulsions—*e.g.*, meningitic, encephalitic, or toxic irritations. Eclamptic attacks occasionally recur in the later years of childhood so closely resembling epilepsy (clinically) as to cause grave confusion. They do often yield to care and treatment so completely as to encourage the opinion expressed by some that there are "late forms of eclampsia." It would seem fair to regard these as mild forms of epilepsy.

Almost anyone of moderate intelligence will readily recognize a well-marked convulsion or even a convulsive tendency; but it is of the utmost importance that the first observer shall carefully note and be able to relate accurately the starting point and phenomena of progress, the degree of severity, and the length of time it has persisted. On these facts will depend a proper diagnosis of the character and seat of the irritation. The slightest twitching of the thumb may indicate irritation or disease near the thumb center. So twitchings of

the eyelid or movements in and around the corners of the mouth may point to central disease. Unilateral convulsions do not necessarily indicate a local lesion, although they form a fair ground for suspicion of focal disease. There is usually some prodromal symptom, more or less brief, such as slight twitchings alluded to in the muscles of the extremities or face, a general restlessness, and startings upon slight irritation from touch or noises. Immediately before the convulsion there is often pallor, a fixity of the eye, or they may be rolled up into their orbits; these slight, isolated movements may pass into convulsive twitchings, extending rapidly over the entire body, or shifting from one side to another, or from one limb to the opposite one along with, or alternating with, movements in the face or head, retraction of the head, or movements of the body over to one side or the other.

A succession of grimaces due to contraction of the facial muscles may be the only early phenomenon, or later the hands may be clenched, the thumbs being buried in the palms; the great toe extended downward—"carpopedal spasm"—or these phenomena again may be followed by a general commotion; frothing at the mouth; disturbed respiration and pulse, slow or rapid, usually irregular; sweating of the forehead or general surface, and blueness of the lips and face. The sphincters may become relaxed, urine and feces being passed involuntarily. After the fit there is usually evidence of prostration, and temporary palsies not infrequently follow, due to exhaustion of the nerve-centers. One attack of convulsions is

commonly followed by others, exhibiting an increasing susceptibility. Convulsions coming on in a child previously well point to some acute disease of exceptional severity, as possibly acute meningitis. Convulsions occurring in most forms of brain disease are not usually accompanied by marked temperature rises, but may exhibit pupillary changes, strabismus, rigidity, or localized palsies.

**ETIOLOGY.**—Convulsions, local or general, arise in excessive and irregular discharges of nerve-centers in the cortex or base of the brain. Nothnagel suggests a convulsive center in the pons. The central gray matter is the source of the spasmogenic impulses.

One of the most popular grounds for explaining the genesis of functional convulsion is Soltmann's doctrine of "physiologic spasmophilia," or "increased disposition to reflex irritation" in infancy. He later assumed in addition to the "*causa physiologica interna*," i.e., the increased susceptibility to reflex irritation, and the "*causa pathologica externa*," i.e., irritation which produces the convulsions, also later a "*causa pathologica interna*," without, however, defining or explaining its nature.

The term "spasmophilic condition" is used by Huebner, and "spasmophile diathesis" by Finkelstein, which last is also called an "exaggerated irritability." The nerve-trunks are shown to be irritable to blows at Erb's nerve points. That on the facial nerve causes Chvostek's phenomenon. Elaborate faradic and galvanic measurements have been made of irritability of nerves by Erb in adults, and by Burckhardt in children.

Abnormalities are pointed out in the galvanic reaction characteristic of the spasmophile diathesis, whereby the forms can be differentiated.

In brief, this spasmophilic attitude affords a graphic name for that condition of "neuronic," "nervous," or constitutional instability which has long been recognized. The question clinicians wish solved is, *How* is this hypersensitive or unstable condition produced? This has been answered by Sajous in his studies of epilepsy. "The tonic spasm is produced," says this author, "in the same manner as the corresponding though more severe spasm of tetanus. . . . Impulses which cause *clonic* convulsions are primarily derived from the cerebral cortex, the spinal system being used as the mechanical intermediary for the production, and are of the nature of voluntary impulses to the spinal system. . . . Clonic convulsions are the results of a temporary and intense hyperemia of the cerebral cortex, due, in turn, to general vasoconstriction (Spitzka). The cortex being a sensory organ, this marked congestion—during which the bloodstream is greatly increased—provokes a storm of impulses to the spinal system—itself hyperemic and oversensitive—which the spinal motor cells convert into motor impulses and transmit to the muscles (which are also hyperemic and overexcitable), thus inducing the clonic fit."

In the normal animal or man the entire spinal gray matter receives spasmogenic impulses from the cerebrum. Excitation of the cortex causes typical convulsions, even after division of the pyramidal tracts, the impulses passing by way of the tegmentum and pons (Prus. Wien. klin.

Woch., Bd. xi, S. 857). Vulpian (C.-r. de l'Acad. des Sci., April 27, 1885) assumes from experiments that the center for epileptic convulsions is located at the base of the brain.

[*Outline of Causal Factors in Functional Convulsions in Infants.*—1. Neurotic inheritance. Heredity plays a small part in causation. When present, the strain is from insane, imbecile, epileptic, hysterical, or other hypoplastic ancestry, or from environmental hypoplasia due to inherited toxemia, syphilis, alcohol, lead, tuberculosis, and possibly certain metabolic faults, as gout.

2. Intra-uterine affections of the brain or circulatory apparatus; gross hypoplastic states, as parencephaly, agenesis corticalis; also congenital cardiac diseases.

3. Causes operative at birth: asphyxia neonatorum, with its disintegrating effects, and meningeal (epidural or subdural) hemorrhage; occasionally trauma exerted on the brain (classic cases of McNutt and Peterson). Effects may be seen soon after birth, or not till after some months does the eclampsia appear. A convulsion within these months should cause search to be made for some prenatal or parturient cerebral insult.

4. Causes operating soon after birth: Atelectasis, infections of the newborn, hemorrhagic diseases of early life; congenital malformations of bile passages by inducing hemorrhages into the brain may be operative; fatigue, exhaustion, emotional depression, fear, anger, shock, blood loss.

5. The most common demonstrable cause of eclampsia in infancy is rickets, or, rather, the hypersensitive condition of the nervous system occurring in rachitic infants, rendering them susceptible to slight reflex irritations; among these are undigested food, foreign bodies or parasites, hyperemic dentition states, adenoids, enlarged tonsils, middle-ear disease, adherent prepuce or clitoris, trauma, incarcerated hernia; sometimes a simple procedure like vaccination may induce eclampsia.

6. Diarrheal diseases (infections) occurring in the first and second years. Convulsions often occur in the course of acute

intestinal disorders consequent to toxemias and meningismus; more frequently in the late stage of subacute or chronic ileocolitis when an hydrecephaloid state has arisen.

7. Meningitis. Tuberculous meningitis arises with some frequency toward the end of the first and during the second year of life, and late in its course convulsions occur.

Convulsions often initiate meningeal inflammations, notably the epidemic form (spotted fever); the simple basilar type of Gee, the pneumococcic and purulent types, or convulsions are seen early in the course.

8. Brain tumors are relatively rare causes of eclampsia; they occur in connection with tuberculomata, gliomata, sarcomata, and syphilomata.

9. Hydrocephalus, whether cognate or acquired, primary or secondary, may induce convulsions.

10. Paleogencephalitis (Strümpell), encephalitis, and meningoencephalitis now are recognized as entities and as causes of infantile hemiplegia, and among the earliest clinical phenomena are oftentimes convulsions, and in half the cases they persist as epileptiform seizures throughout life.

11. Poliomyelitis, though it is usually distinguished from infantile paralysis by its freedom from unconsciousness and eclampsia, does occasionally exhibit these phenomena.

12. Infectious diseases, especially those of severe type. The occurrence of eclampsia early in an infection is due to the severity of the toxemia, or the hypersusceptibility of the individual, or to both; when late in the progress it indicates a complication, such as middle-ear disease, a meningismus, or, as in pertussis, a possible meningeal hemorrhage.

The diseases most often ushered in by eclampsia are: scarlatina, spotted fever, pneumonia, epidemic influenza, tonsillitis, and malaria; even mumps has been so preceded.

13. Nephritis. Acute nephritis may be early accompanied by eclampsia, while in the rare chronic forms the phenomenon is only seen when profound uremia sets in.

14. Severe hemorrhage, with resulting anemia of the brain, may be accompanied by convulsions.



15. Mineral poisons, especially lead.

16. Drugs. Accidental poisoning by strychnine has caused eclampsia.

17. Embolus and thrombosis. The former is rare in childhood, usually occurring in subjects of cardiac disease. Thrombosis, equally rare, may be observed in marasmus, syphilis, or middle-ear disease.

18. Status lymphaticus.

19. Epilepsy.

Epitomized from Taylor, Wells, and McKee, "Diseases of Children," 1913. J. MADISON TAYLOR.]

In infants the nervous system is structurally immature, but in process of rapid development. Even after structural completion, time is required to attain functional stability.

At birth the lower centers only are developed; hence control is limited until the higher centers become competent to exert inhibition. In the earlier months of life convulsions are common, progressively less so after birth to the first year of life, and are more rare after the second year.

In 49 fatal cases the convulsions were ascribed to umbilical infection in 5, to edema and asphyxia in 3 each, and to inherited eclampsia and syphilis in 1 each. In 1 case personally observed the symptoms of general pressure on the brain, evidently due to some supratentorial hemorrhage, persisted for three days and then subsided. Delivery had been normal and brief, with normal pelvis, so that mechanical injury seems out of the question. Esch (Archiv f. Gynäk., Bd. lxxxviii, H. 1, 1909).

It is unusual, perhaps impossible, for a healthy child to suffer from convulsions, unless the exciting cause be overwhelming, such as trauma, an intense irritant, or poison. Convulsions readily occur in children of unstable nervous equilibrium: spasmodic diathesis. This dangerous condition may arise from inheritance or becomes acquired, and is of very

varying degrees. One convulsion predisposes to another, and the habit may become fixed.

Some families are especially prone to suffer ill effects from motor excitations, or their infants offer but feeble resistance to excitants, physical or psychical. Again, individuals vary from time to time, and are rendered acutely susceptible by depressing causes, nutritional and emotional, as well as by the onset of definite disease.

Several causes often act together: vasomotor instability, temporary or prolonged; states of anemia, variations in blood-supply and quality, along with states of certain special nerve irritation, as that of the fifth or gastrointestinal supply (splanchnics). The extremes of heat and cold produce conditions which react in convulsions to relatively slight exciting causes.

What part is actually played by disordered dentition is not determined.

Lancing of the gum over an approaching tooth often relieves obvious irritation which seems to threaten loss of nervous poise. In the same category of doubtful causes may be mentioned the presence of intestinal parasites, where removal is, however, of practical value.

Of the determining causes, by far the most important is the use of improper food, unsuited in amount, kind, or condition to the needs of the young child. This acts often as both fundamental and exciting cause. Milk from a mother or wet-nurse may be vitiated by various causes (fatigue, emotions), or it may act as a medium of poisons (as alcohol), and has been known to cause convulsions.

Other determining causes besides the visceral sensory distribution (gastrointestinal) are such as disordered dentition (fifth nerve); the various infections, especially whooping-cough, syphilis, scarlatina, and the other exanthemata; ptomaines and leucomaines, uremia, malaria, heat, cold, febrile states, burns, fatigue and depressing influences, blood-loss, shock, emotions, fright, anger, etc. Of poisons, some are toxins generated within the organism, and others are from without, such as lead, alcohol, etc.

Interesting cases were reported by D. D. Stewart among a series of children poisoned by lead used as coloring matter in cakes. Meunier reports cases of convulsions caused in nursing where the nurse took large amounts of alcohol. Many of these causes are aggravated by meteorological conditions, especially of hot weather in summer. It has long been believed that convulsions frequently occurred as a prodrome in pneumonia, but Gossage and Coutts show a series of 166 cases with this symptom in only 8, or 4.7 per cent.

Convulsions—and these the more serious ones—are also due to various forms of cerebral disease: hemorrhage, internal pressure as from rapidly increasing hydrocephalus or abscess, and embolus and thrombosis, and, above all, rickets. Only a small proportion of cases of general convulsions, however, are demonstrated to occur in children who have evidences of rickets. In them motor disorders are more likely to be tetany and laryngospasm. The brain presumably suffers from malnutrition or toxemia in all these disorders.

**PROGNOSIS.**—In estimating the dangers resulting from convulsions it

is necessary to consider the nature and extent of the cause. In children of a markedly unstable nervous equilibrium a convulsion may mean little or nothing. Moreover, moderate convulsions occurring in young infants are of small import. Fits appearing as prodromes of acute febrile diseases are rarely serious and may not even indicate an unusually severe attack of the disease. When they occur after the establishment of the characteristic features of the disease they are of deeper significance, and may indicate the oncoming of nephritis, meningitis, middle-ear disease, or other grave complications. Those points on which one is likely to base a serious prognosis are extreme prolongation or frequent recurrence of the convulsions; also profound disturbances of the circulation, stupor, or subsequent prostration.

The old idea that the gravity of convulsions in children depends on the severity of the attacks, their frequency and the age of the child is no longer tenable. The prognosis depends exclusively on whether the convulsions are merely the manifestation of an overexcitable nervous system or are the initial symptoms of organic meningeal or brain disease. This can be determined by the character of the spasms. Clonic spasms are benign; the tonic are of grave import. Clonic convulsions are the expression of the infantile spinal type, as long as this lasts. They occur only on certain soils: an inherited neuropathic taint or an inherited alcohol taint. These clonic spasms can be brought on, with this predisposition, by any mechanical, toxic or physical cause for excitement of the cell. They are a manifestation of bulbomedullar excitation not involving the cortex. Collin and Revon (*Arch. de Méd. des Enfants*, June, 1917).

Gossage and Coutts lay great stress on the facts that the danger of future neurotic manifestations has been underestimated; predisposing causes are of more importance than the exciting causes, and that the slighter exciting causes will not produce convulsions except in children so predisposed. Statistics were produced at the 1899 meeting of the British Medical Association, showing that over one-half of the patients who had exhibited convulsions in infancy suffered from some form of neurosis. And they were not so much to be ascribed to the malnutrition of the nervous system in infancy or to damage during the convulsive stage as to congenital faults of development. This particularly in children of gouty, nervous, or diabetic parents, and it is in whom such a family diathesis is known to exist that any extreme of reflex irritation must be repressed or it will result in a nervous explosion.

#### Convulsions in Status Lymphaticus.

A condition characteristic of infancy and childhood wherein the lymphoid tissues are prone to swelling and hyperplasia has long been recognized, though only recently is becoming understood. This is shown by enlargement of the tonsils, external and internal lymph-glands, the smaller lymph-nodes throughout the body, and by adenoids in the nose and pharynx.

During infectious processes even robust children exhibit acute swellings of the lymph-nodes in the vicinity of the organs chiefly affected; this is commonly seen in the nose, pharynx, and bronchi. The swellings subside usually with much promptitude when the causal process ends. A

certain proportion of children exhibit exceptional vulnerability of the lymphoid tissues, the state of hyperplasia being out of all proportion to the existing cause and continuing long after the cause has ceased to be active; also a trifling, often undiscoverable cause is capable of producing marked engorgement.

Even at birth some infants show an abnormal engorgement of lymph-tissue, especially in the region of the throat, and adenoid vegetations of the pharynx. The influence of inheritance is regarded as important, parents having been susceptible, or of weakened resistance to slight infections, or having been suffering from infection at or near the time of conception of the embryo, or from certain conditions of malnutrition.

Status lymphaticus in its marked forms is quite distinct clinically from the above condition of constitutional susceptibility. None the less, the two exhibit many points of resemblance, are often confounded; hence should be considered together, the primary causes being similar.

The term status lymphaticus is applied to a clear-cut clinical picture, or syndrome, whose pathological factors are upon a common ground of origin.

The clinical manifestations of the status lymphaticus differ from those of the more general susceptibility, are less constant and not characteristic. The two most frequent symptoms are *convulsions* and *attacks of asphyxia*; the most graphic lesion is *marked enlargement of the thymus gland*. Hence it will be seen to exhibit points of resemblance clinically to the *spasmodic diathesis*.

The condition is most often seen in infants between the sixth and the

twelfth month, but may be met with in children of any age (Holt). Since enlargement of the thymus gland is the conspicuous feature, it is essential to acquire a knowledge of the normal size and its variants. Bovaird and Nicoll weighed the thymus in 495 consecutive autopsies in children under 5 years of age. The weight was greatest at birth (7.7 Gm.); during the next period of 5 years the average was 5.9 Gm.—about the same as the average for each year taken separately; excluding instances where the thymus was so large as to seem abnormal, the average at birth was 6.5 Gm.; during infancy and childhood, 4 Gm.

In the condition under discussion,—status lymphaticus,—being considered in its relationship to the “spasmophile diathesis,” the thymus gland is often five to ten times larger than this average size; it has been found to weigh from 30 to 40 Gm., and oftener from 10 to 20 Gm.

Accompanying these cases, the tracheobronchial lymph-nodes are also greatly enlarged, to the size of small cherries and grouped in clusters; those of the mesenteric region may be even larger; Peyer’s patches are prominent; solitary follicles of the small intestine the size of mustard seeds; those of the colon are also prominent. The spleen is usually enlarged, with engorged follicles.

This condition is one of the explanations of sudden death in early infancy, occurring after slight and inadequate causes. The condition may not be recognizable during life in those who live several months, or years, until some acute condition arises, when death occurs suddenly.

The accompanying phenomena are usually attacks of convulsions, or of disturbances of respiration, paroxysms of dyspnea, cyanosis, or asphyxia. Symptoms such as the above may occur and recovery ensue, whereupon status lymphaticus may be suspected.

The causes are not definitely known. Pressure of the enlarged thymus upon the lungs, the trachea, the pneumogastric nerves, or the auricles of the heart has been accredited as the causal agency. Also instances occur when the distressing phenomena described do not arise, yet sudden death follows from some slight cause, an enlarged thyroid for example.

**TREATMENT.**—Combating the immediate phenomena of convulsions becomes less urgent, since it has been shown that the motor commotion, *per se*, does not lead to such disastrous effects as the terrifying spectacle would naturally lead family and physician to fear.

Treatment, then, divides itself into three parts, none of which should be neglected:—

(a) Prevention of the underlying conditions, which includes rational measures along the whole line of regulation of life and conduct in the parents and the individual.

(b) Relief of the distressing phenomena during an attack, “first aid” to the suffering child.

(c) Systematic search for and radical removal of each and every underlying cause; this includes a wide field of investigation, beginning with antenatal conditions—habits, temperaments, and disorders of the parents, especially of the mother; the parturient states and incidents, traumata,

structural defects, sources of reflex irritation, infections, and other toxic factors in the child. Convulsions constitute a symptom, not a disease *per se*. They are graphic and imperative evidences of underlying causes, invariably complex and often obscure.

Prevention can, in large measure, be exercised if the clinician be granted the privilege, whereby alone he can discharge his full duty, of supervising as he may determine needful, all along of antenatal periods, as well as early and periodic supervision and control of life and conduct.

Since the medical adviser is usually called upon only to meet grave exigencies of active convulsions, it is well to form a clear concept of the line of conduct to pursue.

For practical purposes, when we exclude organic affections of the brain, heart, lung, or kidney, the underlying state in infantile eclampsia is usually rickets, or nervous heredity. As to preventive treatment, the instruction of the mother concerning her physical and psychical life during pregnancy, and her protection from emotional storm and mental shock, preventive possibilities of good obstetric knowledge and skill, attention to the hygiene of the baby, with its intelligent medical supervision, are of primary import. Most convulsions should be viewed as wholly preventable occurrences for which parents, caretakers, or lack of medical foresight are to blame. The writer knows no more uniformly dependable agent, in treatment of attacks, than **chloroform**. It is good practice, while the patient is anesthetized, to wash out the bowel with warm normal **saline solution**, permitting several ounces of the fluid to be retained. In a recent case the injection of a second quart of saline solution in a 17-month-old baby brought forth, to the writer's astonished gaze, 8 inches of sewing silk, 82 inches of

darning cotton, and hair from the tail of a rocking horse. **Washing out the stomach** is safer than emetics. These measures should be supplemented with a large dose or broken doses of **calomel**, followed with a single dose of **castor oil** or spiced **syrup of rhubarb**. **Bromide** and **chloral** he recommends to prevent recurrences, the latter drug by the rectal route, with sufficient starch to render it unirritating. Other measures mentioned are the **coal-tar products**, **hydrotherapeutic agents**, **stimulants**, **bloodletting**, **oxygen**, **artificial respiration** and **massage of the heart**, **lumbar puncture of the lateral ventricle**. McKee (Therap. Gaz., March, 1909).

The writer empties the alimentary tract by **gastric** and **colonic lavage** and a full dose of **castor oil** or salts, preferably by the stomach tube. To suppress the convulsions and reduce the likelihood of recurrence nothing gives better results than full doses of **chloral hydrate**. Doses of 7 to 15 grains (0.45 to 1 Gm.) may be given to a child of 2 years and may be administered either orally, by the rectum or subcutaneously. After the child is quieted, a **hot pack** may be given. Newell Jones (West. Med. Rec., May, 1916).

A severe or continued condition of convulsions may produce serious damage to remote organs and tissues. The explosion may be overcome by the **inhalation of chloroform**, which, in such a state of nervous exaltation, is quite safe. To this may be added, with advantage, **nitrite of amyl** and **sulphuric ether**. The mixture I have used for years most successfully in the paroxysm of pertussis is equally applicable here.

℞ *Amyl nitrite* ..... ʒij (8 Gm.).  
*Spt. of chloroform* .... ʒiij (12 Gm.).  
*Ether sulph.* ..... ʒiij (12 Gm.).

It is well to loosen the clothing, or, better, to promptly remove them. Thus, many important points may be

revealed. Often the child will be found in a **bath of hot water**; perhaps **mustard** is added. In the excitement this may have been so hot or irritating as to cause damage, and it is best to remove the child at once, and it may be necessary to study the condition of the skin and apply emollients.

If not in a bath, it is often useful to apply **mustard pack**—which consists of 1 teaspoonful of dry mustard rubbed up with 1 ounce (30 c.c.) of water, 90° to 98° F. (32.2° to 36.7° C.), and added to a quart of hot water, and into this a sheet or bath-towel is dipped and wrapped around the child. After this has been applied for a suitable time, ten or fifteen minutes, or during the continuance of it, a careful search should be made for various sources of reflex irritation. The chief of these may be found in the digestive tract, and the next routine procedure to be recommended is to apply a cleansing **enema**. This enema serves several valuable ends in removing toxic feces or undigested food, and, if hot, aids in stimulating capillary relaxation and diuresis. If the temperature be found high, this can be followed, with advantage, by a cool enema. If subnormal, as is the case frequently in the convulsions following summer diarrheas, a **salt enema** supplies fluid by imbibition, or **hypodermoclysis** may be even better. I have seen lives saved by this. In hyperpyrexia **cold to the head**, an **ice-pack**, is in most cases a useful measure. If congestive states are pronounced, local **bloodletting** by **leeches** is of much use, and is recommended by Baginsky and others. **Lumbar puncture** is a safe measure too, and this I have done with great satisfaction many times.

Convulsions lead to disturbances in the circulation in the brain and meninges which give rise to new convulsions. This vicious circle may be broken up by **lumbar puncture**. Two cases in which this was done successfully in epileptic children. The number and intensity of the seizures were materially reduced by a single lumbar puncture. While the writer does not claim that this measure will prove invariably successful, he believes that the accumulation of seizures is not the work of the primary cause, but of the convulsions themselves, and where this has occurred lumbar puncture may give great relief. F. Schiffer (Klin.-therap. Woch., Bd. xvii, S. 481, 1910).

The writer recommends **atropine** in eclampsia infantum. He used it with marked effect in a 3-year-old girl. The child had had a series of convulsions without apparent cause. Her temperature was high. The paroxysms were becoming serial. Laryngospasm coexisted. The author mixed the contents of an ampoule (0.001 Gm.— $\frac{1}{64}$  grain—of atropine) with 9 c.c. ( $\frac{3}{4}$  drams) boiled water and injected a syringeful (making, he says, about  $\frac{1}{650}$  of a grain—0.0001 Gm.). The symptoms improved almost immediately and no more crises occurred. Rascher (Münch. med. Woch., Jan. 4, 1916).

If the convulsions be unduly prolonged, the use of **morphine** hypodermically is both safe and gratifying. If the first dose (of, say,  $\frac{1}{48}$  grain—0.0013 Gm.—to a 6-month-old baby) is not sufficient, a second may be given in an hour, of double the first dose, and again, in an hour, double of this, if needed. Some regard this as dangerous. Long continuance of a convulsive state may be far worse. It is often the only measure which will successfully check it.

The writer is profoundly dissatisfied with the result of the routine emergency treatment of infantile

eclampsia. The hot bath he discarded long ago, and he is not at all sure that chloroform is an unmixed blessing. In reference to the first, authorities are divided, while the second is acknowledged to be without effect in many cases. Holt has found **oxygen inhalation** successful where all else had failed. In primary laryngospastic eclampsia all treatment by inhalation is useless for the time being, and in all severe cases the function of respiration is seriously compromised.

Death by asphyxia is the most imminent danger, and, as taught by physiology, the more rapidly and completely oxygen is withdrawn, the more tetanized the system becomes. Prolonged suboxidation may be an underlying fault in many cases. **Morphine** as an antispasmodic is certainly more effective than chloroform, and only those object to its use who have never tried it.

To the hot bath there are several objections. A large number of cases of emergency convulsions occur with fever. Hyperpyrexia is most to be dreaded. The writer knows of 2 cases dying in the bath, 1 with a temperature of 109° F. (42.7° C.) and another of 111° F. (43.8° C.). Heat to the spinal column and back of the head is a motor excitant, never a sedative. It is not possible to put a child in convulsions into the bath except in such a way as to immerse the spine. This position is most disadvantageous for dealing with the asphyxia. The abundant mucous secretion and often vomited matter are retained over the larynx, and can only be gotten rid of by placing the child with the face down.

The **cool pack** has none of these objections. In non-febrile cases the **pack** should be **warm**.

In the treatment of cases due to rickets, the **phosphates** with appropriate diet and **hygiene** certainly do good. Phosphorus in oil the author has never tried, believing with Trouseau that "it is a poison, and no medicine." Holt has not been persuaded of its utility, after a fair trial.

**Bromides** and **chloral** are safe and useful as antispasmodics. **Veratrum viride** is especially indicated in acute infections. It has the double advantage of being a spinal sedative, in addition to its utility in febrile conditions.

The writer urges that we go in search of the precise and immediate causative agent or agents responsible for the production of the most common form of infantile eclampsia, the initial pyrexia, and, having found them, direct our therapeutics accordingly. The fine work done by Williams in fastening the guilt of hyperemesis gravidarum upon the liver for failure in its synthesis of ammonia, and that of Howland and Richards in relation to indol and its rôle in recurrent vomiting of children, may well encourage us and serve as guiding stars. Neurin has been thought to be by Donath the autogenetic poison responsible for epilepsy. Suboxidation is certainly an obvious condition present in a large number of cases. E. W. Saunders (Lancet-Clinic, Feb. 6, 1909).

Where there is asphyxia or marked cyanosis, **oxygen** is a valuable agent; this is best administered to infants through a large face-piece and one straight tube. When the bowels are sufficiently cleared, sedatives can be administered by the rectum; chloral and the bromides are most used. For a 6-month-old baby, 4 grains (0.26 Gm.) of **chloral** or 6 grains (0.39 Gm.) of **bromide of sodium** or **strontium**, one or both, may be given; for a baby of 1 year, 6 grains (0.26 Gm.) of chloral and 10 (0.65 Gm.) of a bromide is a suitable dose, to be repeated again at hourly intervals if needed. Authorities differ as to whether an **emetic** should be employed; but if there is reason to believe that there is undigested food in the stomach, this should be used;

and while there may be theoretical objections, I have no reason to believe that harm has been thus caused. Emesis in children is so readily induced that there need be little fear of injurious effects unless excessive stimulus is employed by overdosing with emetics. So soon as the child can swallow, it is well to give a grain or two (0.065 to 0.13 Gm.) of **calomel**, which acts usefully in several ways, even if it does not purge. To produce a full laxation, where this seems necessary, **milk of magnesia**, **castor oil**, or some other active drug can be employed. After having instituted these measures to overcome the activity of the convulsion a thorough search should be made for such sources of reflex irritation as phimo-sis, an approaching tooth, foreign bodies in the nose or ears, etc. As soon as possible, the history of the case should be scrutinized for remoter conditions, such as the existence of a pneumonia, the possibility of the beginning of an exanthema, etc. It must be borne in mind that the occurrence of convulsions is much more frequent and vastly more dangerous during the progress than at the beginning of either pneumonias or the exanthemata. If they arise at the end of an exhausting disease, as of those two just mentioned, or of a prolonged diarrhea, the process is essentially different and will call for other measures. If the urine contains albumin, which must be ascertained without delay, diaphoresis is important; but diuresis must not be neglected, and here repeated injections of **warm salt solution** through the bowel is of value; so also is **hypodermoclysis**. Among the acute conditions which are competent to produce

convulsions in healthy children are injuries to the head, which are liable to be followed by shock and are to be treated as such by **external heat**, **cold to the head**, and **stimulating enemata**. Sunstroke and heat exhaustion call for appropriate treatment; in the former, **external cold** is indicated, and, in the latter, **heat** and **stimulants**, of which among the best is **coffee**. An accidental cause may be mechanical obstruction of the upper air passages, and, if apnea is the chief difficulty, the introduction of a **tongue depressor**, drawing the tongue firmly down and forward, may remove the symptom almost immediately. Lastly, it must not be forgotten that convulsions may be a phenomenon of impending death, when it is impossible to expect to relieve them; although it is oftentimes admissible to make use of **strychnine** hypodermically and in large doses, and of other forms of stimulation.

**Phosphorus** in the convulsions of infancy exerts a more decided calmative influence on the nervous system in infantile eclampsia than does chloral or bromides. After carefully examining and cleansing the gastrointestinal tract, the drug is administered for two or three days, in doses usually employed in rickets. Lange (*Semaine méd.*, No. 3, 1900).

**Calcium** increases the resistance of laboratory animals to strychnine. Dogs and cats bore without harm the fatal dose of strychnine by the mouth if they were given from 100 to 180 c.c. of a 5 per cent. solution of calcium lactate or acetate at the same time or three or four minutes later. Later than this, the calcium salt by the mouth had to be supplemented by intravenous injection in order to save the animals. Similar action in increasing the resistance of the animals was apparent when the calcium salt was given with or soon after the



animals had been injected with blood-serum from patients with eclampsia or uremia. Comparing these with clinical experiences sustains the assumption that a lack of calcium is a prominent factor in the pathogenesis of convulsions, and that supplying large amounts of calcium may render inactive the substance causing the convulsions. T. Silvestri (*Gaz. degli Ospedali*, Nov. 23, 1911).

### **TETANY (INTERMITTENT TETANUS, LITTLE TETANUS, TETANILLA).**

Tetany is a motor neurosis, or "spasmophile diathesis." The spasms, or convulsions, appear suddenly, are occasionally preceded by sensory or constitutional disturbances; they may last several hours, or even days, to reappear after remissions of equal length, and are often accompanied by alterations of sensibility in the affected limbs, without loss of consciousness. It is far from common, yet not rare.

**SYMPTOMS.**—The symptoms of tetany are to be divided into those of the attack and those of the period of latency. The onset of the paroxysms may be preceded by sensory phenomena, headache, nausea, mental depression, vertigo, irritability, and occasionally transient blindness (see C. S. Howard: *Amer. Jour. Med. Sci.*, Feb., 1906, quoting Kussmaul, Bouveret, Trevelyan, and Cunningham); but is often sudden and without warning. Consciousness is preserved throughout the attacks. The sensations are usually vague, tingling pains in the forearms and legs, followed soon by a tonic convulsion of the extremities or a stiffness of the muscles. This spasm is most marked in the upper extremities, giving rise to such a pronounced rigidity that it

is almost impossible to overcome the resistance by active effort on the part of another. When the rigidity is mild the child may exert enough will-power to overcome the forced position long enough to use the hands for grasping. Toward the end of an attack relaxation occurs. The face muscles may become so involved as to produce disfiguring grimaces. Rarely compression spasm may cause expulsion of urine, or disturbances of deglutition, of the pupils, of the thorax; hence dyspnea. Occasionally there is anuria. Skin changes are at times seen: erythema, purpura, or eruptions. Occasionally, the adductors of the thighs and arms are involved, causing the arms and legs to be drawn together; more rarely the muscles of the neck are involved, and also those of the trunk. True pathognomonic symptoms are spontaneous intermittent paroxysmal muscular contractions. The most common seat of these contractures is in the muscles of the forearm, the fingers being flexed at the metacarpophalangeal joints, while the phalanges are extended, the thumbs being strongly adducted, the wrists acutely flexed, and the hands turned to the ulnar side. The position of the hand is called the "accoucheur's hand" or the "writing hand." Other attitudes are, however, occasionally seen, such as a firm clutching or even complete extension of the fingers. The forearm may be flexed upon the arm, the arm adducted to the shoulder.

If, or when, the lower extremities are involved, the thighs may be adducted, the legs extended or flexed; the toes are apt to assume the position of talipes equinus. The spasms may affect the muscles of the abdo-

men, the back, the diaphragm, and the thoracic muscles; hence inspiration is endangered and cyanosis may result, even consciousness being lost (Weiss). Trismus is rare; yet, opisthotonos is not exceptional. Other muscles may be affected, as of the eyes, the esophagus, the pharynx, the larynx, or even the bladder. Laryngeal spasm is a common accompaniment of the disorder. Naturally, this degree of overtonicity may cause muscular pains. The degree of spasm varies, and also its length. It may last from two minutes to two hours or more. As has been said, the involvement of the muscles is symmetrical. Cases have been reported of one side only, or unilateral for a time. In the contracted muscles fibrillary twitchings have occurred; clonic movements almost never. Tremor is common. The spasm begins in the periphery, not from within outward, as in tetanus; nor are the masseters early affected, as in that more serious malady; nor is reflex excitability high; nor is the spasm continuous, as in tetanus. During the intervals the patient is comparatively comfortable. The muscles are often tender and sore, and they are weakened. The intervals are variable: usually a few hours, or it may be several days or weeks. Edema may occur, developing gradually in the dorsum of the hands and feet. Often there is cutaneous hyperesthesia. Other symptoms are those of Trousseau, already mentioned. This is the fact that, if, during the passive interval, the limb be grasped in such a way that the great nerves or arteries which lie along the under surface of the limbs are pressed upon forcibly, the characteristic cramp can be made to

return. It may require some continuance of this pressure to elicit the phenomenon, but when it is present it is regarded as pathognomonic of tetany. "The constriction, which must be great enough to produce cyanosis of the distal portion of the extremity, must be kept up for from one to several minutes before convulsion makes its appearance and the procedure is attended with some pain" (Thiemich). This is not always to be obtained: in perhaps only one-fourth of all cases. Its value is great in demonstrating the existence of "latent tetany": a form in which there is at no time a clearly marked contracture. Chvostek's sign is rare in children. It consists in an extraordinary susceptibility of the nerves in tetany to mechanical impressions. A blow with a percussion hammer over the facial nerve produces a twitching of the angle of the mouth or of all the muscles of the facial distribution.

The third important symptom of tetany, known as Erb's sign, is a greatly exaggerated electrical excitability of the nerves. Weak faradic or galvanic currents produce muscular contractions in excess of the normal response. Cathodal-closure contractions are found with small currents, but also with moderate currents; also cathodal-closure tetanus and anodal-opening tetanus, which are not observed in any other condition.

The most convenient test, and one which usually suffices in an affected person, is increased mechanical excitability, a simple touch, a light pressure on a nerve, being enough to produce contractions in the muscles supplied by it. It is less painful to

the subject than to induce an attack by pressure on a large trunk or artery (B. Sachs).

Sensory phenomena are few; there are no disturbances of cutaneous sensibility. Headache, vertigo, nystagmus, and tinnitus aurium are described as coexisting. Temperature elevation is only rarely produced, but may be present because of some underlying condition.

Respiration is not, as a rule, affected. Dyspnea is sometimes produced by fixation of the muscles of the thorax and the diaphragm. The pulse is often increased in frequency. The urine is rarely affected; it may be increased in amount. Nephritis occurs occasionally. There are seen, at times, certain nutritive disturbances affecting the hair, nails, etc. The reflexes do not show any characteristic alterations.

The duration of an attack of tetany is most variable. There may be many remissions of greater or less severity, of shorter or longer periods of abeyance.

**DIAGNOSIS.**—The clinical picture of tetany is thoroughly characteristic; the condition should be easily recognized.

The position of the hands; the fingers grouped together or held rigidly in this or some other attitude, as in extension; the legs oftentimes affected as well, or both arms and legs firmly adducted, should instantly excite suspicion. On investigation the sign of Trousseau would reveal the condition even during the periods of latency; that of Chvostek (irritability to slight mechanical stimuli) and that of Erb (electrical excitability as described) should make the diagnosis clear.

In the writer's series of 318 electrical tests on 118 infants, 10, or 3.1 per cent., gave evidence of extreme or cathodal hyperirritability. Of the middle-grade or anodal irritability giving response to cathodal closure and anodal closure alone, below 5 milliampères, there were 101, or 31.8 per cent. With cathodal closure and anodal opening alone present, below 5 milliampères, he found 50, or 16.6 per cent. With both cathodal closure, anodal closure, and anodal opening, less than 5 milliampères, there were 40, or 12 per cent. The occurrence, then, in his series of abnormal reaction or increased electrical response according to Escherich's definition was 193, or 61 per cent. H. B. Wilcox (Amer. Jour. of Dis. of Children, June, 1911).

The writer describes the facialis phenomenon as a sudden contraction or spasm of the muscles of the nose, eye, and forehead, supplied by the facial nerve, when a sharp tap is given over a point midway between the zygomatic arch and the corner of the mouth on one side. At times fibrillary twitching around the eye and nose take the place of the combined spasm of the muscles. This phenomenon is of great value in the diagnosis of infantile tetany and in the prevention and treatment of laryngismus stridulus and allied spasms. H. Neumann (Deut. med. Woch., Bd. xxxviii, S. 813, 1912).

Morse, of Edinburgh, regards the one symptom pathognomonic of tetany: the spontaneous intermittent, paroxysmal conditions of the muscles of the forearms.

The *leg phenomenon* of Schlesinger has been confirmed by Glassner in 1 adult, and by Gottlieb in 1 of 2 children. The writer reports positive findings in 2 adults, negative in 2 infants. He believes that it is entirely due to mechanical stimulation of the sciatic nerve by stretching, and is entirely analogous to the Trousseau phenomenon, which Fränkl-Hochwart by animal experimentation has shown

to be of nervous, not vascular, origin. In both adults, pressure at the sciatic point elicited the typical position of the foot (talipes varus or equinovarus) as well as did Schlesinger's procedure—flexion of the thigh with extended knee. Alexander (Deut. med. Woch., Nu. 22, S. 1030, 1910).

The writer's *tongue phenomenon* is a deep groove that forms in the side of the tongue when it is tapped. Tapping on both sides of the tongue or on a spatula lifting up the tongue induces a waist-like constriction across the tongue. This tongue sign he found constantly in tetany in adults. He has also been impressed with the persistence of the muscular contraction in tetany after mechanical irritation of certain muscles. F. Schultze (Münch. med. Woch., Oct. 31, 1911).

Not all the characteristic symptoms are seen in each case, and the absence of some one or other does not vitiate the diagnosis.

**ETIOLOGY.**—Tetany arises in certain localities, and is not seen again for long periods. It may become epidemic (Bruns). The condition was described by Trousseau originally, who discovered the important symptom known by his name, viz., that an attack could be induced in an affected subject by compressing the arteries and the nerve-trunks. Tetany occurs in both adults and children, in about equal frequency (B. Sachs), but most cases are seen in the very young. Holt says it is usually seen in early infancy, between the fourth and tenth months. Barthez and Sanné found it more often in children and most in infants. Griffith found 66 per cent. under 2 years of age.

Case of a healthy couple with 5 children, all the children developing tetany before they were 1 year old, three dying in convulsions before they were 2 years old, and the other

still with severe tetany. There were no signs of tetany in any of the children until after they were weaned. Necropsy of 1 of the children failed to reveal anything pathological in the parathyroids. Schiffer (Jahrbuch f. Kinderheilk., May, 1911).

In 91 examples of typical spasmophilia by the writers, a familial factor was evident in 25, that is, in nearly 25 per cent. It usually was manifested in the appearance of tetany in 2 or more members of the family. In some the spasmophilia was latent and required special tests to bring it into evidence. In some families alcoholism or grave constitutional disease or neuropathic stigmata were manifest in parents or brothers or sisters. Rachitis, status lymphaticus, adenoids or merely enlarged glands often accompanied the symptoms of spasmophilia. The boys outnumbered the girls in the children with spasmophilia. A familial occurrence is thus shown to be not the exception but the frequent rule. Pincherle and Pollidori (Rivista di Clinica Ped., Apr., 1918).

The disorder is much more common among the children of the lower classes, and those whose surroundings are unwholesome. It almost always follows upon depressing conditions, overexertion, or recognizable disorders or diseases, especially the transmissible ones; hence its pathology is to be regarded as a toxemia. In all these conditions tetany, as Sajous pointed out in 1907, is an accessory phenomenon due not to the autotoxins or bacterial toxins they add to the blood, but to a single class of spasmogenic agents in all cases, i.e., toxic products of imperfect catabolism due to deficient activity of the thyroid and parathyroids.

Study of the recent literature concerning the tetany of nurslings. As to the work done on the parathyroids and thyroids, it cannot be shown that

these bodies show any constant anatomical alterations, but a functional insufficiency is highly probable, dependent on an inborn inferiority. The weight of evidence still shows that poverty of calcium salts is in some way associated with spasmodophilia, but other factors must be involved, i.e., spasmodophilia means more than simple defect of lime salts. As to the association of tetany with other organs and functions, a certain parallel exists between tetany and ergotism, and the former has been brought in relation with the circulation in the blood of a hypothetical vasoconstricting substance—perhaps more than one. Thus some cases of tetany could be explained by exogenous poisons and intestinal autointoxication, while others must depend on strictly endogenous poisons, as in tetany from extirpation of the parathyroids. Meyer (*Berl. klin. Woch.*, June 24-July 1, 1912).

The writer's extensive experience has convinced him that an over-excitable weakness of the nervous system due to lack of calcium is responsible alike for tetany in young children and the spastic constipation, colic pains in the domain of the mesenteric plexus, enuresis and nervous pallor in older children and for asthenia in adults. Two familiar facts in the history of tetany are its connection with the parathyroid bodies and with the metabolism of calcium. Abnormally low calcium content of the blood seems to accompany tetany and to be found exceptionally frequent with the nervous peptic and trophic disturbances of older children and adults. He tabulates the findings in 53 children from early infancy to 14 years old; in the 23 with abnormally low calcium content in the blood, 4 had pronounced tetany and all the others belonged to the group of constitutional spasmodophilic asthenia in children of all ages. H. A. Stheeman (*Nederl. Tijdsch. v. Geneesk.*, May 5, 1917).

It is frequently associated with rickets. Rarely it has resulted from

a known poison, such as lead, alcohol, or ergot. It is in some way connected with disturbances of calcium metabolism, as shown by McCallum and Voegtlin in 1908. It occurs as a finality to, or associated with, structural diseases of the nerves, and is known to result from extirpation or destructive lesions of the parathyroid and thyroid glands. That the parathyroid gland secretes a something the absence of which is followed by a perturbation of the normal nervous balance has now been demonstrated.

Experimental and clinical data sustain the view that extreme neuromuscular excitability in children is due in part to lack of normal proportions of calcium in the tissues. It is the only one among the cations indispensable for the human organism investigated to date which influences the electrical reactions by its varying concentration. At the same time there must be other factors involved, as the varying lime content does not explain all the phenomena observed, although the theory of a deficiency in lime as the direct cause of the spasmodophilic syndrome explains several essential features. E. Reiss (*Zeit. f. Kinderheilk.*, July, 1911).

The most attractive theory as to the real causes underlying the manifestation of tetany is that of Eschrich and Yanase. It is the only explanation of the phenomena of tetany that seems to be founded on experimental data. Seeing the close similarity of infantile manifest tetany with that which is seen after operations on the thyroid gland, Eschrich has ventured the opinion that they are both identical. They are both dependent on some lesion of the parathyroid glands or epithelial bodies which in some way comprises the efficiency of these glands in counteracting, as they do normally, the toxins in the circulation acting on the nervous system. The result is that the toxins act unrestrained, and

produce the manifestations of tetany, a so-called parathyreopriva. As a corollary to this is the theory that the calcium salts in some way may be responsible for the immediate exhibition of tetany. Escherich tried through his school to prove that the irregular distribution of calcium salts resulted in the production of tetany, and that this distribution was disturbed by an interference with the function of the parathyroid bodies. How this may be brought about Escherich, through Erdheim and Yanase, showed that in cases in which lesions due to tetany, such as hemorrhagic cysts and parenchymatous changes, were found in the parathyroids in cases of tetany with sudden death. The launching of this theory has been the stimulus to a large amount of investigation of the parathyroid glandules in infancy. One of the contentions of Escherich that hemorrhage in the gland may occur as the result of the great strain on the infant during birth has been taken up by Grosser, Betke, and Auerbach, who have stated that hemorrhages in the parathyroids have been found in a number of conditions, infectious and toxic, in which tetany was absent, and in cases in which the electrical reactions during life were normal. In a recent case of tetany of his own, in which the parathyroids were carefully examined by Oppenheim, the only changes found in the glandules were peculiar dilatations of the lymph-spaces. The whole matter of the influence of lesions of the parathyroids in causing tetany still remains to be closely studied. Certain it is that of all the hypotheses of the disease thus far broached it is not only the most attractive, but one which harmonizes most with our knowledge of tetany elsewhere than in infants. Henry Koplik (*Med. Record*, Sept. 16, 1911).

Any exhausting disease is a possible cause of tetany in those predisposed to this form of motor disturbance.

## **PATHOLOGICAL ANATOMY.**

—No constant nor characteristic lesion has been found present at autopsies in tetany. Serous exudation into the cervical cord and into the ventricles of the brain, sclerotic changes, spinal extradural hemorrhage, atrophy in the ganglion-cells and nerve-fibers, and proliferation of the neuroglia are among the conditions found, as enumerated by Dercum.

In an analytical study of 6822 children, with special attention to determining the nature of tetany and its relationship to rickets and laryngeal spasm, Cassel found 60 cases of tetany. The nutrition was good in 14, moderately good in 13, poor in 23, and bad in 10. All presented spontaneous intermittent spasm, which could be induced by pressure upon the large nerves and vessels of the affected parts. In all but 3 the facial phenomenon was present. Only 2 had laryngeal spasm, and both of these presented craniotabes in addition to other symptoms of rickets. Without exception, the children were nervous and slept badly; 14 presented a rise of temperature; in 9 the disorder was the result of complicating conditions, and in the remainder it arose without apparent cause. In 21 cases digestive disturbance preceded or accompanied the tetany, in 5 there was chronic dyspepsia, in 43 digestive disorder, in 6 obstinate constipation, and in 4 habitual vomiting. Rickets was present in 52 of the 60 cases; in only 8 there was no trace of rickets. Tetany was seen throughout the entire year, although the largest number appeared to occur in the spring and late autumn. There was no suggestion of an epidemic occur-

rence of the disease, nor was there any relation as to frequency between tetany, rickets, laryngeal spasm, and craniotabes. Cassel concludes that tetany is neither a complication of rickets nor of digestive disturbance, but is dependent upon favorable conditions of living, improper nutrition, and bad air. Holt says most cases occur in winter.

The evidences point to the conclusion that tetany is a disorder of the spinal and bulbar gray matter and the peripheral nerves, somewhat generally distributed, and of toxic origin. It arises, preferably, in those who have suffered from exhausting conditions, depressing circumstances, or acute diseases, or all three.

**PROGNOSIS.**—The prognosis of tetany, on the whole, is favorable. Most cases recover. Especially is this true since the newer remedies, especially parathyroid glandules, have been added to our resources.

**TREATMENT.**—In the treatment of tetany, causal factors should always be remembered. In children rachitis should be treated with **phosphorus** and **codliver oil**. In gastric tetany surgery must remedy the underlying mechanical conditions that are the cause of stagnation, dilatation, and intoxication.

Emotional disturbances, exposure to heat or cold must be avoided. Meat should be excluded from the diet. Milk is well tolerated and may be of advantage by reason of its large calcium content.

By a careful study of the relation of diet to infantile tetany in 4 cases, the writer was able to confirm the statement made by Finkelstein to the effect that some substance dissolved in the whey of milk acts harmfully in tetany. In 1 of his cases, "with sur-

prising regularity," the tetany became worse or better, according as the whey was added to or withdrawn from the food, and this regardless of the quantity of food and of its content in fat and sugar. There is doubtless in the whey some material which acts in an irritating manner, producing an increase of the irritability of the peripheral nerves. The removal of whey from the food gives a diet which is non-irritating in these cases, but which frequently must be supplemented with sedatives in order to bring about a proper reduction of the spasmophilic condition.

The curds of milk from which the whey had been removed did not seem to have any irritating power in the author's cases. The writer, therefore, fed children afflicted with tetany with a suspension of these curds, which was found to be most satisfactorily prepared as follows: The milk is brought to a boil and then cooled to 107° F. (41.6° C.). Chymogen, a teaspoonful to the quart, is added and the temperature kept at 107° F. (41.6° C.) for half an hour. The milk is then strained through a cheesecloth and allowed to drain for one hour. The curds are finally put through a sieve with fine mesh, and suspended in a solution of arrowroot flour of the strength of 1 level tablespoonful to the quart. C. G. Grulee (*Archives of Pediatrics*, Jan., 1912).

The sources of tetany were studied by the writer. Experiments with the different elements of milk albumin in feeding children inclined to spasmophilia, showed that the albumin did not seem to have anything to do with this morbid tendency. On the other hand, giving the children the whey alone, freed from all albumin, brought back the symptoms of spasmophilia in children who had apparently thrown it off after milk had been dropped entirely. Larsson (*Svenska Läkare Handl.*, Sept., 1917).

The essential cause of tetany being an intoxication, our duty is to enhance all functions which tend to en-

hance catabolism of the toxics and to eliminate them. For the latter purpose, moderate **catharsis** and **dialyphoresis**, **saline irrigations**, and the **ingestion of large amounts of water** are helpful in the elimination of metabolic poisons. As a detoxicant, **thyroid preparations** are frequently given with benefit. Kocher has seen disappearance of tetany symptoms under thyroid and thyroid preparations, though Fränkl-Hochwart and others have seen no benefit from thyroid preparations; rather the reverse—a fact attributed by Sajous to the use of excessive doses. The efficiency of **calcium** and **parathyroid** administration is now recognized.

In severe acute cases, whether post-operative, idiopathic, or of gastric origin, from 45 to 75 grains (3 to 5 Gm.) of **calcium lactate** in 400 or 500 c.c. (13½ ounces to 1 pint) of **saline solution** should be given intravenously. The action of calcium on control of symptoms is evanescent and the dose may have to be repeated in twelve or twenty-four hours. The **parathyroid proteid** prepared according to the directions of Beebe is of equal value and should be given hypodermically, 1 c.c. (16 minims) of a 1 per cent. solution every three or four hours for two or three days and then less frequently. Good results from both calcium and the parathyroid proteid in chronic cases have been reported by Beebe, MacCallum, Halsted, Putnam, Poole, and others. Dried extracts of the gland have proved less efficacious.

Pal reported marked benefit from the use of **pituitary gland** in a boy with severe tetany. Ott and Scott, from experiments on cats, conclude that pituitary extract given hypoder-

mically is equal to calcium in the control of spasm. In man the 20 per cent. infundibular extract that is now on the market may be given intramuscularly, from 7 to 10 drops (0.4 to 0.6 c.c.) three times daily.

**Transplantation of the parathyroids** may be of great service in the future in chronic cases of tetany. Christiani has transplanted parathyroids in rats and cats and found the grafts successful after periods of two to five years. Von Eiselsberg transplanted a parathyroid obtained during a goiter operation into the rectus muscle of a woman suffering from chronic tetany the result of a total thyroidectomy that had been done twenty-seven years before. The tetanic seizures disappeared except for occasional slight spasms of the glottis, and electrical irritability became normal (Moffitt).

Tetany in pregnancy and parturientcy does not differ essentially from that of the other forms. Because of the parathyroid origin of tetany, the implantation of parathyroids suggests itself, but experiments on animals have shown that after a certain time changes take place in the transplanted organs so that permanent results are rare. **Parathyroid preparations** have given good results in some cases, but have failed in others. The same is true of **thyroid treatment**. **Calcium chlorate** or **lactate** are valuable. In a personal case the writer obtained excellent results from the administration of 1 Gm. (15 grains) of calcium lactate 4 to 6 times a day. **Milk** and **vegetables** contain calcium and therefore are useful. Guggisberg (*Correspondenzbl. f. Schweizer Aerzte*, Dec. 15, 1917).

If the spasmodic phenomena are excessive or painful, it is well to proceed in the same line as in dealing with convulsions. The inhalation of



**chloroform**, or a mixture of **chloroform**, **nitrite of amyl**, and **ether** (3, 2, and 3), will hold the spasm in check. Sedatives, such as the **bromides**, or **chloral** may be used.

The change from cows' milk to carbohydrate-starch diet is often, as shown by the writer, a life-saving measure with spasm of the glottis and general convulsions in the spasmophilic diathesis. The prompt influence from this change in diet may differentiate disturbances from this cause when the symptoms otherwise suggest meningitis or otitis media. It is also useful in controlling the spasms in whooping-cough. Langstein warns, however, that the starch diet may have a pernicious effect with infants suffering from severe gastrointestinal disturbances. **Breast milk** is alone permissible in these cases. Fischbein (*Therap. Monats.*, May, 1910).

The disorder is one chiefly of prodigality of motion—as I have constantly maintained in dealing with disorders of motion, such as chorea—and is always followed by exhaustion (fatigue neurosis); hence the fundamental need for all such states is absolute **rest** for both body and mind. The next indication is to remove all sources of peripheral irritation. Finally, nutritive **tonics** will be required in most cases, and to be maintained for a long time.

**Gastroenterostomy** has been resorted to successfully where the disorder was due to retention of the ingesta in the stomach.

Details of the 21 cases of gastric tetany in which an operation was done. The consequences were 17 complete cures and 1 material improvement; 3 of the patients succumbed, notwithstanding the operation. This is a mortality of 15 per cent., while the mortality was from 71 to 77 per cent. and over in Loeb

and Albu's recent compilations of cases in which reliance was on internal measures alone. The writer advocates operating without further delay when the dilatation of the stomach is due to organic changes; extreme stenosis of the pylorus is frequently accompanied by tetany. A **gastroenterostomy** puts an end at once to the stagnation of the ingesta, with the consequent irritation of the vagus, entailing continuous hypersecretion, and thus does away with the irritation liable to start the tetany. K. Wirth (*Centralbl. f. d. Grenzgebiete d. Med. u. Chir.*, Nov. 26, 1910).

### MUSCULAR HYPERTONIA.

General muscular hypertonia without spasmophilia, symptomatic hypertonia or persistent spasm, persistent spasm or "myotonia of the newborn" (Hochsinger) have been recognized (since Czerny and Moser's articles) as a symptom of severe nutritional disturbance. The convulsions vary in intensity, but are never intermittent; occur only in children a few weeks or months old, and rarely in the period which furnishes most tetanic cases; almost always arise in those exhibiting some acute septic process, or other evidence of cerebral irritation or palsy. The pathogenesis is not clear.

**TREATMENT.**—The treatment is that for the primary disease, and the general lines indicated for tetany.

### PSEUDOTETANUS.

Pseudotetanus, observed first by Escherich, occurs in children from 4 to 16 years of age. The subject, usually a boy of good heredity and previous health, begins to complain of stiffness in the legs, rigidity of the spine, which spreads rapidly to the upper portions of the body, back, and head, till the patient lies in complete extension, immobile as wood; all the

muscles of the trunk, legs, and neck are in a state of maximum contraction. The face also becomes affected, presenting an expression which Soltmann describes as "of a person blinded by a bright light"; the teeth are clinched tightly. During sleep some relaxation occurs, but never complete. Sensory or psychic stimuli induce paroxysms of hypertension with pain, opisthotonos, spasm of the diaphragm, dyspnea, etc. The duration of the disease is from three to six weeks; recovery is slow, being complete in about a month longer.

The nature of pseudotetanus is not clear. Pfaundler considers pseudotetanus to be an infectious disease closely related etiologically to rheumatic tetanus.

**TREATMENT.**—The treatment is similar to that of tetany, described above, and removal of the cause.

### AUTOMATIC MOVEMENTS IN CHILDREN.

Automatic movements may occur in the following diseases:—

I. Anomalous epilepsy.

II. Hysteria of childhood. General, quasipurposful. Hysterical, salaam, and hysterical eclampsia rotans.

III. Athetosis (athetoid movements in asthenic conditions).

IV. Automatic rhythmical movements. These are better displayed in a table:—

Automatic rhythmical movements.	Head-nodding and shaking	Movements of assent.
		Negative move- ments.
	Gyrospasm.	
	Head-banging.	
	Eclampsia nutans, or salaam convulsions.	
	Eclampsia rotans.	

V. Tic convulsif.

VI. Induced automatic movements.

It may be advantageous to examine each division carefully and endeavor to define diagnostic features and differences, and in a few instances it is possible to assign a cause.

**ANOMALOUS EPILEPSIES.**—In these forms there is exhibited a most marked display of automatic imperative movements. By relating a typical case a good concept can be formed: A boy aged 17; weakly, nervous, and irritable. The attack begins usually with a sharp cry and without further development. The patient commences to run aimlessly through the street, usually at a good speed. If stopped by anyone, he may struggle violently, or even pass into epileptic convulsions, from which he awakens exhausted, asks for water, and promptly goes to sleep. His apparent oblivion to the external world, the inability to make any impression by speaking to him, his avoidance of collision with objects and people, and particularly his absence of remembrance when he awakes of events taking place during the attack lead one to regard it a pure case of secondary consciousness of automatic and, usually, centric origin.

Some cases run round and round, only stopping to fall exhausted and senseless to the floor. Another variety manifests no motor excitation whatever; the patient will suddenly, in the midst of some rational action, wander quietly off by himself, accost persons on the street, and, at times, threaten to do violence if the one addressed does not agree to some absurd demand on his part. Then comes the awakening. The patient does not know where he is or how he

got there, and exhibits signs of exhaustion and thirst.

**Treatment.** — The treatment of these cases is the same as that for idiopathic epilepsy.

### HYSTERIA OF CHILDHOOD.

—In referring here to hysteria, we shall simply consider that type in which there are observed automatic movements.

Hysteria of childhood is a condition which frequently simulates anomalous epilepsy, and at times it is only with extreme difficulty that a differentiation can be made. Like epilepsy, there is often an initial scream, which differs in quality from that of epilepsy, and which usually is not given until the patient is aware that she (usually a female) has an audience. The patient then falls to the ground in a way that she will not be hurt. At times a very fair representation of opisthotonos is presented. Engorgement of veins about the head is frequently noted, and more or less active tonic spasm is present. After this follows a condition of relaxation, with wild quasi-purposeful movements of the arms; broken short sentences, explosions of passion and profanity, weeping, laughing, and grinding of the teeth often follow. The larger and more sympathetic the audience, the more varied and emotional will be the manifestations.

Anesthesia, paralyses, hallucinations, and ecstasies have their turn, and gradually the patient quiets down to normal. The notable feature in these cases is the imperative and purposeful movements, mostly confined to the arms, which the patient will often assert, during the attacks, she cannot possibly stop.

[Alfred Reginald Allen, my assistant, aborted a most pronounced one of these seizures in a hospital case by an **hypodermic injection of sterilized water** with a dull needle. In another case of the same kind he used **hypnotism**, the sudden command, successfully. J. MADISON TAYLOR.]

**Athetosis** should never be confused with any other automatic condition, and all that need be said of it here is that when hysterical, or secondary to some functional or mild disorder, a good prognosis may be given; otherwise it should be guarded.

**AUTOMATIC RHYTHMICAL MOVEMENTS.**—In this term are broadly included head-nodding, or movements of assent; head-shaking, or negation movements (synonymous with *spasmus nutans* and *nictitatio spatia*); gyrospasm; head-banging; *eclampsia nutans*, or *salaam convulsions*, and *eclampsia rotans*.

Head-nodding and head-shaking are manifestations which appear in the infant at any time between the ages of two and eighteen months. It is sometimes preceded by injury to the head, as might be occasioned by a slight fall. But the condition has appeared so many times when such history cannot be elicited that it would lead one to think injury not an essential factor in the etiology. In most cases the nodding and shaking are preceded a week or ten days by nystagmus, which may be vertical or horizontal, or vertical in one eye and horizontal in the other. At times there is only a uniocular nystagmus. When the nodding and shaking appear they are usually limited to a few attacks a day, which tend to increase in number. There sometimes appear cases in which there is almost constant nutans of a mild type, with strong exacerbations. In the great

majority of cases the movements seem to be accentuated when the attention is distracted, or if the child makes an effort to hold his head still. Caillé (Arch. Ped. Soc., 1889) reports cases where movements ceased when attention was fixed and also if eyes were bandaged. His treatment of the case was to keep the eyes bandaged for some weeks—only removing the dressing to flush out the conjunctivæ. Recovery ensued. The pupils are usually dilated, the eye-grounds normal. The few cases in which fundus changes have been found are coincidental. Occasionally there occur periods of unconsciousness, with marked deviation of eyes to right or left (Hadden).

Very frequently there is a history of rickets, and the rosary and other features are well marked. In most of Hadden's cases there occurred, as an early symptom, the throwing back of the head and looking at objects with partially closed eyes.

Head-nodding is much rarer than head-shaking. Occasionally these alternate in the same patient.

If it be desirable at this time, with our limited knowledge of this condition, to classify them under any particular heading, hysteria in childhood would seem to present the greatest claim, for in hysteria there are frequently salaam movements, pure and simple. Until more is known of the essential nature of those conditions, and their relation to the few different lesions which have been found in the brain at death, it will be an impossibility for us to go further than to offer surmises as regards a classification. They are so frequently associated with defective mental development that the suspicion of their being

significant of some deep-seated developmental error is urgent.

When a combination of motor impulses by their cross-action imparts a rotary motion to the head, this is known as gyrospasm (Peterson). These spasmodic conditions sometimes increase during sleep. According to Peterson, the number of excursions of the head in these affections rarely exceeds two or three a second. The child may only have an attack during the night, or it may be so persistent that it suddenly awakens him every time he composes himself for sleep.

In eclampsia nutans and rotans there is a bowing, or salaaming, movement of the neck. Hadden differentiates those conditions from head-nodding and head-banging, and calls eclampsia nutans and rotans a variety of epilepsy.

In anomalous or aberrant forms of epilepsy there is a salaaming, but also there are other signs of epilepsy.

A perfectly analogous condition to all the above automatic imperative movements may be induced by suggestion under hypnotism.

Other motor neuroses—such as habit chorea, habit spasm, convulsive tics, echolalia, coprolalia—are dealt with elsewhere.

A curious case was reported by Sée (St. Barthol. Hosp. Rep., 1886) in which the brother of a case of head-banging was similarly affected while sleeping in the same bed. The symptoms disappeared immediately on the separation of the children.

**Treatment.** — The treatment of head-movements is **change of air and climate, nutritious food, and out-of-door life**; in short, improved hygiene, careful search being made for and

correction of any source of reflex irritation, such as postnasal adenoids, adherent prepuce, phimosis, dental disturbances, intestinal disorders, intestinal parasites, etc.

Most of the sufferers are too young to warrant the correction of errors of refraction, though they may readily exert an influence. The condition of any of the aforesaid irritations may solve the difficulty. It is safe, nevertheless, to begin at once on a treatment by sedatives. **Bromides, valerian, chloral**, etc.; nutritive tonics, such as codliver oil, iron, phosphorus; fatty and albuminous foods, and the organic nuclealbumins are likewise indicated. Depression of the inhibitory centers governing the anterior cornual cells of cord has been suggested, with **quinine** as an inhibitory stimulant. (See Treatment of Convulsions.)

**Progressive Torsion Spasm of Childhood.**—This condition, which according to J. Ramsay Hunt (Jour. Amer. Med. Assoc., Nov. 11, 1916) has been recognized only 6 years, is characterized by peculiar spasms, hypertonus, and hypotonus of the muscles of the trunk and extremities, and a series of twisting and torsion movements. The spasms are increased by activity and decreased by rest. Gait and station are mainly affected and the tendon reflexes are present, but difficult to elicit. The reported cases and 6 personal observations are reviewed by the writer. All of these facts brought out that the affection is limited to childhood in its onset, occurs almost exclusively among Russian or Polish Jews, is progressive, and involves the sexes equally. The lower extremities and lower part of the trunk are most frequently and extensively involved and the muscles supplied by the cranial nerves are never

affected. Remissions and exacerbations are rare. There is characteristically a disturbance of harmony of muscular action with hypertonus of some and hypotonus of other muscles. Lordosis and crescent feet are usually present. There is a reversal of voluntary movement; thus an attempt to extend a flexed foot results in increased flexion and *vice versa*. The condition is probably due to some organic central lesion situated below the corpus striatum.

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Philadelphia.

**COOLIE ITCH.** See DERMATITIS.

**COPAIBA.**—Copaiba is the fluid oleoresin obtained from several trees of the genus *Copaifera*, which are found in South America. This fluid exudes after the bark of the tree is wounded, and has a pale-yellow or brownish-yellow color. It is a more or less transparent and viscid liquid, the consistency varying with the season, and has a peculiar aromatic odor and a persistent, bitter, acrid taste. The specific gravity varies from 0.95 to 0.995.

**PREPARATIONS AND DOSE.**—*Copaiba*, U. S. P., is insoluble in water; slightly soluble in absolute alcohol, carbon disulphide, fixed and volatile oils, and completely soluble in ether and chloroform. It contains a volatile oil (*oleum copaiba*), 48 to 85 per cent., and a resin, 15 to 52 per cent., from which copaivic acid can be made. The dose is 15 minims (1 c.c.).

*Oleum copaiba*, U. S. P. (oil of copaiba), is a volatile oil distilled from copaiba. It has a pale-yellow color, a peculiar aromatic odor, and an aromatic, slightly bitter, pungent taste. Its specific gravity is 0.895 to 0.905 and it is soluble in 2 parts of alcohol. It may be suspended in mucilage of acacia or in yolk of egg, and cinnamon or peppermint water with tincture of orange or ginger may be used to mask the taste. It may be given in capsules. Dose, 8 minims (0.5 c.c.).

**PHYSIOLOGICAL ACTION.**—Applied locally, copaiba is slightly stimulating to the skin and mucous membranes.

Taken internally, copaiba leaves a disagreeable taste in the mouth and gives an offensive odor to the breath. Medicinal doses continued for a long time or large doses are irritating to the stomach, and cause digestive disturbances, loss of appetite, offensive eructations, and frequently vomiting and purging. The gastric untoward effects are, in part, avoided by administration during meals.

It has a stimulating and disinfectant effect on the various mucous membranes. Its particular action is upon the mucous membrane of the genitourinary tract. It gives a peculiar aromatic odor to the mucous secretions and urine.

Copaiba acts as a diuretic and has an antiseptic action on the urine, thus tending to retard the growth of microbes and to promote healing of lesions in the genitourinary tract. Large doses of the drug are irritating to the kidneys, causing inflammation of these organs, with scanty urine, containing albumin, blood, and casts.

The continued use of copaiba frequently causes a measly rash and itching of the skin, and sometimes erythema, urticaria, or a bullous eruption. The rash may be very limited, but occasionally covers the entire body, suggesting measles. It disappears without desquamation in four or five days after the withdrawal of the drug.

The drug is eliminated by the skin, bronchial mucous membranes, and kidneys.

**THERAPEUTICS.**—Copaiba may be applied locally, as a stimulant and antiseptic, in chronic skin diseases, **psoriasis**, **lupus**, and **leprosy**. The drug has been considered favorably in the treatment of **chilblains** and **frost-bites**, the parts to be bathed every night with warm water, and the drug then freely applied. This treatment should be kept up for about one week. It is also said to be of value when applied to the surface of old **ulcers**, Stephens recommending the use of equal parts of copaiba and resin cerate for this purpose. It may also be applied to the urethra and vagina in **chronic gonorrhea**.

Internally, copaiba is a standard remedy in the treatment of **gonorrhea**. The use of the drug is begun as soon as the initial severity of the condition has passed, and the bowels have been freely opened. Oc-

asionally, copaiba may be given as an expectorant in **bronchitis**. Whittall uses equal parts of copaiba and castor oil by injection in the treatment of **chronic cystitis** of women. It is also said to be of value sometimes in **psoriasis**, **ascites**, **chronic intestinal catarrh**, and **chronic diarrhea**. Its use is restricted on account of its unpleasant taste, and its liability to produce disagreeable eructations, to derange the digestion, or to produce eruptions of the skin. H.

**COPPER** (cuprum) is a brilliant metal of a peculiar red color, widely distributed, and never used as such in medicine, but usually as the sulphate. Copper sulphate appears as large, transparent, deep-blue crystals, odorless, and having a nauseous, metallic taste. It is soluble in 0.5 part of boiling water, 2.2 parts of cold water, 3.5 parts of glycerin, and 400 parts of alcohol. It is incompatible with alkalis and their carbonates, lime water, mineral salts except the sulphates, the iodides, and most vegetable astringents.

**PREPARATIONS AND DOSE.**—*Cupri sulphas*, U. S. P. (copper sulphate, blue vitriol, bluestone), is given in the dose of  $\frac{1}{2}$  grain (0.01 Gm.) as an astringent, and 4 grains (0.25 Gm.) as an emetic.

Other preparations sometimes used, but which are not official, are the acetate, the arsenate, and the ammoniate of copper, and the oleate, which is employed as ointment.

**PHYSIOLOGICAL ACTION.**—Applied locally to a mucous membrane, copper sulphate acts as a powerful astringent and antiseptic, and to an ulcer, as a mild caustic.

Taken internally a full dose of copper sulphate acts as an emetic by its local action. Small doses of the drug are astringent. Copper sulphate exists in minute quantities in the blood, and, when taken into the body and absorbed, it is said to have an affinity for the hemoglobin, forming what is called "cuprohemol." Small doses are said to have a tonic action, especially when given in combination with quinine. It is absorbed from the stomach, intestines, mucous membranes, and small wounds, and stored up in the liver, small amounts being found also in the spleen, kid-

neys, and thyroid gland. It is eliminated by the liver, kidneys, and the salivary and intestinal glands.

*Action of colloidal copper* on blood studied in man and rabbits. In the human subject 5 c.c. (80 minims) were injected subcutaneously. The red cell count and hemoglobin percentage were at first lowered, then returned to normal on the seventh or eighth day. The leucocytes were also decreased at first, but then rose abruptly, being more than doubled on the third and fourth days. They returned to normal on the fifth to the eighth day. There was also observed an early polymorphonuclear leucocytosis and lymphopenia, followed by an increase of the lymphocytes and large mononuclears to a point above normal. These results are similar to those previously obtained by Achard and Emile-Weil in experiments with colloidal silver. H. Chabanier, L. Rollin, and E. Chabanier (*Presse médicale*, Feb. 5, 1913).

**ACUTE POISONING.**—Upon ingestion of toxic doses of copper sulphate, there is severe pain in the stomach and a metallic taste in the mouth. This is followed by vomiting and purging, the passages first consisting of the contents of the intestines, then of mucus, and finally of blood. Severe headache and profuse salivation occur. The pulse and respirations are weak, and the skin cold and clammy. Coma, delirium, or convulsions, followed by paralysis, usually follow. Death may occur in a few hours or a few days, and is due to exhaustion.

Acute poisoning with salts of copper is rare, and 3 cases reported by the writer are therefore worthy of note. In 2 copper sulphate was taken, and in the third the substance was acetate of copper. In all instances the poison was taken for the purpose of suicide. In the first case, in which acetate of copper was taken, the tongue and pharynx were unaltered. The mucous membrane of the esophagus, on the other hand, was easily detachable, and had a greenish-blue color. The stomach contained 200 Gm. (6½ ounces) of

a greenish-blue fluid mixed with mucus, with an acid reaction, but having no specific odor. The mucous membrane of the stomach was thickened, hard, and dry, as if tanned, and blue in color. There were a few ecchymoses and hemorrhagic erosions on the rugæ. The peritoneal surface was unaltered. The large and small intestines contained a fluid similar to that found in the stomach, and the mucous membrane of these parts was also hard, dry, and of a blue color. The other organs showed no marked changes. In the second case, a woman took a quantity of a concentrated solution of sulphate of copper. Death occurred in a few hours.

The stomach contained 500 Gm. (1 pint) of an acid, greenish fluid. The mucous membrane was thickened, contracted into rugæ, and was as if tanned. There were a few ecchymoses on the crests of the rugæ. The intestines presented similar appearances, although not so well marked as in the stomach. The other organs of the body showed nothing characteristic. In the third case, in which a young woman took copper sulphate, there were no pathological changes in the stomach and intestines, and the diagnosis of the poison taken was made from the clinical observations and the color of the vomited matters.

The writer points out that the negative results of the post-mortem examination in the last case are quite in accordance with experience in regard to other poisons, in which, in cases of undoubted poisoning, no pathological changes have been observed. The first 2 cases indicate that copper salts have a corrosive action attributable to their power of coagulating albumin. The coloration of the mucous membrane of the whole alimentary tract makes the question of diagnosis easy, and the author observes that this color in the case of sulphate of copper is greenish, whereas in the case of acetate of copper it is rather blue. Horoszkiewicz (*Vrtiljschr. f. gerichtl. Med.*, Berlin, 1903, Heft 1).

**CHRONIC POISONING.**—Although not common, chronic poisoning by this drug sometimes occurs. The green color of different canned vegetables in common use by the public is often due to preparation with copper.

Method of testing copper salts for coloring green peas: Green peas were boiled in a solution of copper sulphate until they had absorbed all the copper in the solution. Then fresh peas were boiled in water for the same length of time. Next a few of the colored peas and a few of the uncolored were boiled for three minutes in a 10 per cent. solution of sulphuric acid. Each sample was then poured out on a white saucer. The pulp of the colored peas as well as their skins always retained the green color after this test in a degree which was proportionate to the quantity of copper present, while the peas that had not been colored turned a brownish or grayish black. By this method so small a quantity as 0.025 Gm. ( $\frac{3}{8}$  grain) of copper in a kilogram ( $2\frac{1}{4}$  pounds) of peas was detected. A. V. Nikitine (Vratch, March 11, 1900).

Copper may also enter the food from cooking utensils made of this metal. The skin and hair of workers in copper or brass often have a greenish tint, and a green line may be seen along the upper border of the teeth. Colic and diarrhea, or acute febrile attacks of gastrointestinal catarrh, may occur, and may be followed by local paralysis. Other symptoms sometimes observed are anemia, wasting, headache, tremor, vague pains, pharyngeal and laryngeal catarrhs, and profuse perspiration. The occurrence of these various symptoms is said to be partly due to the deposit of copper dust on the skin, hair, and teeth, and partly due to the lead, arsenic, and other poisons so frequently associated with copper, but cases do occur in which the symptoms of chronic poisoning are due to copper alone.

Fines of £2 with £2 2s. costs and £1 with 2s. costs were inflicted in London recently upon a wholesale grower for selling preserved peas which contained 3.402 grains (0.22 Gm.) of sulphite of copper per pound (500 Gm.) and beans

which contained 4.067 grains (0.26 Gm.) per pound (500 Gm.). Medical evidence was given by the acting medical officer, who explained the cumulative effect of repeated doses of sulphate of copper, and pointed out that, though it might be administered mechanically, the maximum dose in such a case would be considerably less than that contained in a pound of peas or beans as sold by the defendant. When only a small amount of copper was used it entered into combination with the chlorophyll, forming phyllocyanate of copper. There was no direct evidence that phyllocyanate of copper in minute quantities was injurious to health, although dogs fed on this substance became paralyzed, which paralysis ultimately caused death. When copper was used in such large quantities, however, as those stated in the analyst's report the copper entered into combination with the pith or substance of the pea or bean, forming leguminate of copper. A. D. Cowburn (Lancet, Aug. 20, 1904).

Copper smelting is a dangerous occupation, because of the tremendous amount of dust which rises from the fire when feeding the furnace, and men cannot work long in this position; they contract both the lighter and more severe pulmonary diseases; where the ore runs a high percentage of lead and arsenic, cases of severe poisoning occur and paralyses are not uncommon.

As zinc occurs with sulphur, lead, and arsenic as impurities, the effects of zinc roasting is about similar to that of copper, with the addition of the so-called ague seizure and its accompanying symptoms. Sicard (Med. Record, Aug. 5, 1905).

Copper poisoning, some years ago, was much more common when the metal was relatively cheaper and hence was more largely employed in making cooking utensils for family use. Many cases of poisoning were directly traced to the contamination of food prepared in a *copper utensil*, and by chemical investigation it was found that, unless these utensils were kept very bright and clean, they would give rise to



poisoning, by the formation of verdigris, a basic copper acetate.

Recently in the village of Pekin, Niagara County, New York, at the annual commencement exercises, *ice-cream* was served, the custard of which had been made the night before and thoughtlessly left standing overnight in a large copper boiler. The ice-cream was made the following morning and that afternoon served to between 70 and 100 children and adults in attendance at the exercises. Before the exercises were over, a number were taken ill. They hurried to their respective homes, followed by others who did not feel well. Soon the entire party had gone and many became seriously ill. No one died, but some had a hard fight to win against death. The physicians agreed that the ice-cream was the cause of the trouble, and that, had the custard stood a little longer until the poison had grown stronger, many deaths would have followed.

Copper is sometimes added to *pickles* to make them of a brighter green color, a fraud which can readily be detected by placing a blade of a knife or polished piece of steel in the liquid; if it contains copper, there will be a deposit of metallic copper upon the iron in the course of a few minutes. It is held that the very small amount of copper that would be introduced into the system by eating such a pickle would be only a mere fraction of a grain and not enough to cause any symptoms. No matter how small the amount of copper may be in the pickles, yet no one will be satisfied to know that he is eating such an active poison.

A far more dangerous source of poisoning is found in the *wall-paper* pigments containing copper arsenite, which is very poisonous. It is not only the green colors that are dangerous, but all vivid colors, such as scarlet, crimson, or lake. It is especially velvet or embossed papers that are likely to be loaded with pigments, and these should never be used for a dwelling house unless first tested and found to be free from copper or arsenic by the

ordinary tests for those poisons. Editorial (Medical Bulletin, July, 1908).

Case of chronic copper poisoning observed by the writer from a dental bridge in a young woman. The alloy in the bridge was only eight carat fine. E. Harnack (Deut. med. Woch., July 23, 1914).

**TREATMENT.**—In treating a case of *acute poisoning* by copper, the chemical antidote, **potassium ferrocyanide**, should be given at once, followed by the administration of **demulcents**,—eggs, milk,—and the **stomach** then **washed out with alkaline solutions** unless vomiting is already present. Large doses of **potassium iodide** should be given. **Counterirritation over the abdomen** and **opium** should be employed to relieve pain.

In cases of *chronic poisoning* 15 drops of dilute **phosphoric acid** should be given before meals. Large quantities of **milk** should be ingested, and the bowels thoroughly evacuated daily, preferably by the use of either the **sodium** or **magnesium sulphate**.

**THERAPEUTICS.**—As a caustic, copper sulphate is less painful and milder in action than silver nitrate. It may be used locally on **indolent ulcers** and **exuberant growths**, as well as on **syphilitic ulcers of the throat**. It is also of value as a local application in the various forms of **ulceration of the mouth**. The copper crystals may be applied to **granular lids**, and a  $\frac{1}{4}$  per cent. solution may be used in **conjunctivitis**.

The writer has used copper citrate in 109 cases of eye disease. The writer experimented with various germs, and found that a solution of 1:9143 killed the *Staphylococcus pyogenes* in from three to six and a half hours; the *Bacillus pyocyaneus* in seven hours, etc. Ointments containing copper citrate in use for a month were found sterile. The remedy was used in the following forms: (1) A 5 or 10 per cent. powder with sugar. (2) A 5 to 20 per cent. ointment with vaselin, lanolin, or glycerin, according to Arlt's formula (copper citrate, 5 to 20, and glycerin ointment, enough to make 100). (3) In the form of pencils, containing from

10 to 20 per cent. of the active substance in gum arabic, starch, dextrin, sugar, distilled water, and glycerin, to make a mass. (4) In the form of washes, in water, 1:9143. The author has employed this remedy in fresh **trachoma**, in **pannus tenuis**, in **pannus crassus**, in **corneal opacities**, and in **chronic conjunctivitis**. He obtained good results in 62.5 per cent., 35.2 per cent. of the cases giving no results, while in 2.02 per cent. the disease became worse. Krotoff (Roussky Vrach, April 26, 1903).

Strong solutions also have a mild hemostatic effect and may be used in **hemorrhages from small wounds**. Weak solutions may be used for **dressings in septic conditions**. Internally, copper sulphate is one of the most effective astringents in the treatment of **chronic diarrhea**.

As a therapeutic agent copper is not appreciated at its true worth—as the most efficient remedy at our disposal for the treatment of a whole group of diseases, some of which occasionally give us much concern. Copper owes its medicinal desirability to a remarkable selective action. It is highly poisonous to the lower forms of plant life and has very few undesirable effects on the higher forms of either plant or animal life.

The effect of  $\frac{1}{24}$  grain (0.0027 Gm.) per hour of copper sulphocarbonate on **choleraic diseases** is marvelous; all of the serious symptoms abate in a few hours. When using the copper nothing is used to control the diarrhea directly unless it seems to be too debilitating. Then a little camphorated tincture of opium is added and perhaps some cinnamon. The writer has prescribed copper sulphocarbonate (phenolsulphonate) over 900 times in all forms of choleraic and **diarrheal diseases** with uniform success and satisfaction. Its greatest usefulness is in the prevention of all of these diseases, the most important of which with us is, of course, **typhoid fever**. By disinfecting the **typhoid carrier**, it ought to enable us eventually to get rid of the disease. C. Wyckoff Cummins (Jour. of the Med. Soc. of N. J., June, 1912).

It may also be used as an emetic, but, on account of its irritating action, the stomach should be promptly washed out if the drug does not produce vomiting. On account of this action some observers restrict its use as an emetic to cases of **phosphorus poisoning**. Small doses of copper sulphate are said to give relief in the **vomiting of pregnancy**, and it has also been recommended in the treatment of **syphilis**. In **chronic nervous diseases** the long-continued use of the sulphate is sometimes efficient, and it has also been used in **anemia** and **chlorosis**.

Dilute solutions of copper salts have a marked destructive action on many bacteria. Of these salts the sulphate is most active. This is probably due to the fact that it undergoes electrolytic dissociation more readily than the others. The amount of sulphate to be used in the water should be from 1 part in 750,000 to 1 part in 5,000,000, depending on the character of the water.

Extremely dilute solutions of copper sulphate as an algicide in reservoirs and ponds overgrown with algæ destroy typhoid and cholera infection, as shown by laboratory investigations, and many practical applications of the method have been made in various parts of the country, with results varying from complete success (against algæ) to utter failure. Each body of water should be studied separately as a distinct problem. Objection has been made in various quarters to the use of even so minute an amount as 1 part of copper sulphate in 5,000,000 of water, on account of possible ill effects therefrom, although the daily ingestion of small amounts of that salt is held, rightly or wrongly, by most authorities to be free from danger to health. But within a very short time all traces of copper disappear from the solution. This is not true with all waters, for it is the experience of the writer and of probably many others that evidence of its presence may still be found some weeks after the treatment. The authorities of Elmira, N. Y., added not 1 part in 5,000,000, but 1 in 700,000, or about seven times as much. Half a liter (pint) of the water, taken thirty

hours after treatment and concentrated by evaporation to a single cubic centimeter (16 minims), yielded not the slightest trace of copper, it having been precipitated after performing its office. In this instance, it may be noted, there occurred complete destruction of the algæ and a diminution of more than 90 per cent. in the number of bacteria. In some cases objection has been raised that, although the algæ are destroyed, the turbidity persists; but generally the killing of the algæ is followed by their rapid disintegration, with disappearance of turbidity. In other cases a more serious objection is that, while certain species are destroyed far more easily than others, and although overgrowth by these may prevent the latter from undergoing extensive multiplication, the disappearance of the easily destroyed species may remove the obstacles to and be followed by an overgrowth of an equally objectionable but more hardy species. With regard to the bactericidal power of colloidal solutions of copper, there are already many remonstrances that the original statements appear not to be justified. Among those who report against placing any reliance upon this form of treatment of public water supplies for the destruction of typhoid infection is Prof. John H. Long, of Northwestern University, who made an investigation of the subject in behalf of the Illinois State Board of Health. In a communication from Dr. J. A. Egan, the secretary of that board (*Journal of the American Medical Association*, October 15, 1904, p. 1157), Professor Long is quoted as saying: "While in sterilized water in contact with copper the death rate of typhoid bacilli is high, their persistence for two or three days, and the possible persistence for longer periods in larger amounts of water, render the method impracticable for use in rendering a suspicious water safe for household use." Attention is called to the fact that typhoid bacilli disappear from ordinary water in from one to ten days without treatment, and that, therefore, "the disappearance of the bacilli forty-eight hours after seed-

ing in a copper vessel may be due not only to the action of the copper, but to the natural destruction of the bacilli in water." Moore and Kellerman (*U. S. Dept. of Agriculture, Bureau of Plant Industry, Bulletin 64, 1904*).

Results of an investigation conducted for the purpose of determining the following points: (1) the use of copper alone, or in combination with lime, for the destruction of mosquito larvæ; (2) as a deodorant. Sulphate of copper combined with lime is more effective as a destroyer of mosquito larvæ or as a deodorant than when used alone. Against mosquitoes the combination is effective not on account of its toxicity, but because it rapidly removes from the water the organic matter on which the larvæ feed. This method of destroying mosquitoes is therefore of limited applicability. As a deodorant the mixture is the most valuable agent we have at present. It is cheap, harmless, and easily made. It acts rapidly on both solids and liquids and its effects are permanent. Doty (*Med. Record*, Jan. 21, 1905).

On analysis the pool water in the Taylor Gymnasium at Lehigh University was shown to contain, just after filtration and before any one entered the pool, 10 bacteria per cubic centimeter, and no colon bacilli; after 40 men had been in the pool, although all the preliminary sanitary precautions had been taken, the water contained 5300 bacteria per cubic centimeter, 200 of which were colon bacilli. Copper sulphate can be used in germicidal quantities without any disagreeable results. The writer found that about  $\frac{1}{20}$  (0.04) part of the copper sulphate to a million parts of water, used every day, kept the water pure. S. J. Thomas (*Jour. Amer. Med. Assoc.*, Sept. 25, 1915).

The writers found experimentally that very low concentrations of copper will, if sufficient time is allowed, kill or inhibit the growth of many pathogenic organisms. A dilution of 1:100,000 prevented the growth of tubercle bacilli in the test tube.

Some organisms (notably *B. prodigiosus*) were found markedly susceptible, while others (*staphylococcus aureus* and the molds) were very resistant, surviving 15 minutes' exposure to a 5 per cent. solution, a high concentration. DeWitt and Sherman (Jour. of Infect. Dis., Apr., 1916).

*Colloidal copper* will quickly destroy certain bacteria; should copper vessels or plates be used to destroy bacteria in water they must be kept highly polished or the bactericidal properties will be greatly reduced. Gildersleeve was unable to find evidence of copper, ingested in small quantities for long periods, having a detrimental action on the health of an individual.

Colloidal copper has recently been tried in the treatment of **cancer** by Loeb, Lyon, McClurg, and Sweek. As these authors state, it is, however, too early to make any definite statements as to the ultimate fate of the patients they have so far treated successfully.

H.

**CORN.** See SURGICAL DISEASES OF THE SKIN.

**CORNEA, DISORDERS OF THE.**—The majority of disorders of the cornea are of importance because they give rise to opacities or to irregularities of the corneal curvature that may impair or cause the loss of vision.

**KERATITIS.**—Inflammation of the cornea. When purulent it is nearly always due to pyogenic organisms which invade the cornea from without.

**Varieties.**—The varieties of keratitis are the parenchymatous or interstitial, neuropathic, malarial, dendritic, herpetic, punctate, disciform, filamentous, phlyctenular, bullous, pannous, traumatic, striate, suppurative, mycotic, and xerotic keratitis.

**Symptoms.**—The most constant symptom is opacity; and this may be the only objective symptom present. It may vary from the slightest in-

crease of the haziness that is visible in the normal cornea, under strong oblique illumination, with a good magnifier, to complete opacity through which no trace of the iris or pupil is visible. The opacity always causes impairment of vision, proportioned to the extent to which it invades the part of the cornea in front of the pupil.

Redness is manifest, not usually in the cornea itself, but in the vessels at its border, which supply it with nutrient fluid; and the enlargement of which gives rise to the pericorneal zone. In chronic keratitis, however, as during the later stages of corneal ulcer, and in pannus, trunks of considerable size may be seen arising from the vessels at the corneal margin extending on the cornea, and dividing, to be distributed to the superficial corneal layers. In interstitial keratitis great numbers of extremely small vascular loops extend from the margin into the deep corneal tissue. As the inflammation goes on to resolution, the corneal vessels atrophy and in most cases entirely disappear. In a few cases parenchymatous keratitis runs its course without at any time exhibiting vascularization of the cornea or hyperemia of the pericorneal zone.

The pain of keratitis is usually severe. It may be that of a foreign body in the eye, a smarting, burning, or severe aching pain. It is commonly attended with photophobia, which may become intense, and with increased lachrymation. Swelling may occur in corneal inflammation, but it is inconstant and of little consequence.

Loss of substance, ulceration, is a far more important symptom. In

many forms of inflammation the resulting ulcer is the most significant and most serious symptom. Its characteristics are closely identified with the variety of keratitis, and will therefore be considered under the special symptoms peculiar to each variety. In all corneal ulcers, however, extension usually occurs by the breaking down of an infiltrated area; and, while active, the surface of the ulcer, when wiped with a pledget of cotton, lacks the smooth reflex of the normal corneal surface. Before the ulcer begins to heal, the points of infiltration disappear and the ulcer is said to be "clean." Its surface, too, becomes coated with epithelium, and, although not so even as the normal corneal surface, appears to have the same polish. As the loss of substance is made good with new-formed tissue, the lack of transparency in the scar-tissue gives rise to an opacity which will be most noticeable some weeks after all signs of active inflammation have ceased. Such corneal opacity and the possibility of perforation of the cornea and its sequels are the special dangers of ulcerative keratitis.

**Parenchymatous keratitis** begins with photophobia, slight redness, and irritability of the eye. Opacity appears faintly near the middle of the cornea, involving the deeper layers; increases from day to day, and extends toward the periphery. Then at the border, usually the upper or lower border, the cornea becomes opaque, and fine loops of deep vessels push out in it and extend gradually farther toward the center, giving the tissue they invade a characteristic "salmon" color. In rare cases the disease runs its course without any vascularity of the cornea or redness of the peri-

corneal zone. Iritis or choroidal inflammation is liable to attend this form of keratitis, and may be manifest before the opacity of the cornea wholly hides the iris and pupil. Usually both eyes are affected; but sometimes with an interval of months or years intervening before the second is attacked. The course of this form of keratitis is essentially chronic, usually running through several months and sometimes years before it subsides. The corneal surface often becomes quite uneven, but is rarely ulcerated. The disease generally affects both eyes, usually occurs during childhood or youth, but may be met in early adult life, or even later. The patient frequently presents other evidences of inherited syphilis, particularly the Hutchinson teeth, or the nasal deformity; or the symptoms may be those that are grouped under the term scrofula, or that indicate tubercular disease in other parts of the body. In some cases trauma seems to be the exciting cause.

Annular keratitis is a transient stage in the course of parenchymatous keratitis, which otherwise does not differ from the usual diffuse parenchymatous keratitis. This form, on account of its typical clinical aspect, deserves a special place among parenchymatous keratitides. It is not an exclusively syphilitic disorder. Vossius (*Klin. Mon. f. Aug.*, Bd. xliii, i, S. 657, 1910).

**Iodine** hypodermically is recommended by the writer in keratitis, scleritis, and uveitis. He gives 10 minims (0.6 c.c.) of a 2.5 per cent. solution, in fatty combination, in the flank once or twice weekly. R. Kerry (*Ophthalmol.*, xii, 327, 1916).

The primary lesion in simple herpetic keratitis is situated in the ciliary ganglion. The most useful local remedies are **holocaine** and

**atropine**; often 1, sometimes both, are supplemented by **dionin** instillations. Recovery is somewhat tedious. S. Theobald (N. Y. Med. Jour., Aug. 5, 1916).

**Neuropathic keratitis**, or neuro-paralytic keratitis, is usually marked by diminished sensitiveness of the cornea to touch as compared with the sound eye. It also may be attended with iritis, but is commonly confined to one eye. The liability to it increases with age, and there is likely to be other evidence of involvement of the ophthalmic branch of the fifth nerve, as herpes zoster, neuralgia, or distinct paralysis. Curiously enough, it is possible to remove totally the Gasserian ganglion, and, by careful protection of the eyes during the first few weeks, to escape any neuropathic keratitis. There is very likely to be ulceration, although this may not occur, and the ulcer may become infected and the keratitis lose its characteristic features. Its course is quite chronic; but healing, usually with more or less opacity, mostly occurs in three to six months.

In making the diagnosis the important factors are the corneal sensibility; the appearance of the lesions, especially after staining with fluorescein; the injection of the eye, the intraocular tension, the size of the pupil, the subjective symptoms, and the occurrence of herpetic skin eruptions. For the first, a piece of thread, as recommended by Fuchs, is the most satisfactory in his experience, the cut end being rubbed over the surface, the pressure being increased as necessary. The same route should not be followed twice, as this might increase the sensibility. The tendency is for it to be lessened in this disease; cases in which it is increased are too rare to be of much importance. It is always a surprise to the patient to find that the affected eye is less sensitive than the other, and he may answer incorrectly

for psychologic reasons. This fact, however, makes the test more reliable when hyperesthesia is found. There may be subjective pain of a neuralgic character referred to the eye or its neighborhood, sometimes extremely severe and often entirely absent. It may be experienced in the outset of the attack only, but sometimes persists. Frequently all that is complained of is dimness of sight. On the whole, however, the subjective symptoms bear no relation to the severity of the case.

The treatment has usually been rather unsatisfactory, though occasionally in mild cases an **occlusive bandage** is effective. Within the last two years the writer has used a treatment, which he adopted as being based on rational theory, with good effects. It occurred to him that, since neuropathic keratitis was due to an irritative lesion of a sensory nerve, anesthetizing the terminals of the nerve by a local anesthetic would lead to recovery. As such an anesthetic he chose **holocaine** for apparently unimportant reasons, such as that it was slightly antiseptic and that its solutions remain sterile. He employed a 1 per cent. aqueous solution at intervals of two hours, a bandage being essential to the treatment. As a rule, a mydriatic was not prescribed unless there was a well-marked iritis. He has also added **hyoscine hydrobromate**, in the proportion of 1 to 300 to the holocaine solution, with good results, though he cannot say that atropine might not have done as well. He has now treated over 100 patients in this way and has not yet seen a patient fail to improve. Recurrences occasionally took place, calling for general treatment also. Since arsenic seems to have an effect on nerve-tissues and the results of its administration have been very satisfactory, he now gives it in all non-traumatic cases in which some other general treatment is not indicated. His custom has been to order 2 drops (0.12 c.c.) of **Fowler's solution** three times a day, increasing 1 drop (0.06 c.c.) daily till 10 drops (0.6 c.c.) is reached and then continued for a month or longer,

care being taken to watch for symptoms of arsenic intoxication. F. H. Verhoeff (Jour. Amer. Med. Assoc., July 17, 1909).

The *trophic and traumatic hypothesis* has been held to be the most satisfactory explanation by Parsons, Head, Sterren, Wilbrand, and Sanger. They all admit that there are such things as trophic nerves in the corneal epithelium, and that these nerves play an important part in the protection and safety of the cornea from foreign bodies and accidents. They insist that there must be a central distribution of the nerve-roots or ganglion-cells to explain the keratitis. It is quite true that many of these patients who are in the throes of trifacial neuralgia are willing to sacrifice an eye with the hope of relief from pain, but further perfection of the technique may render removal of the Gasserian ganglion unnecessary. W. B. Weidler (N. Y. State Jour. of Med., Oct., 1912).

In acute coryza and gastro-intestinal disturbances, herpetic lesions at the periphery of the cornea may occur. Facial herpes being neuropathic, these lesions are probably likewise so. Rosacea keratitis is also regarded by the writer as a neuropathic keratitis. He does a partial *periotomy* to interrupt the injurious nerve impulses. In 15 cases he uniformly secured prompt healing, without recurrence. F. H. Verhoeff (Arch. Ophth., xlv, 148, 1916).

Cocaine locally applied may open the door to germ activity because of its action upon the protecting epithelium. The first effect of the drug, when instilled in the eye, is a marked constriction of the blood vessels and a drying of the superficial epithelial layer of the cornea. There are probably more cases of ill effects from the local use of cocaine than is realized; keratitis is the rarest of the results, but the "watery eye" due to overuse of cocaine, by women especially, to relieve the burning and itching of chronic conjunctivitis or the edematous conjunctivitis which occurs in those subject to the vas-

cular changes which culminate in giant urticaria, is the most common. R. I. Lloyd (Annals of Ophthal., Oct., 1917).

**Malarial Keratitis.**—Keratitis quite neuropathic in its clinical character may arise in malarial persons in connection with fifth-nerve lesions, especially malarial neuralgia. But in a more specific form, as in a linear branching ulcer, it also occurs with impaired sensibility to touch, and some opacity of the affected part of the cornea.

Malarial keratitis, which consists in a branching linear ulcer of the cornea best manifested by staining with fluorescein, with variable surrounding infiltration, is an unusual complication of malarial disorders. It occurs most commonly in late summer and autumn, is never multiple, is very rare in the chronic forms of malaria, rarely occurs in both eyes and not infrequently causes serious damage to the cornea. One attack predisposes to others, but not invariably. The lesions are probably trophic, and that they follow the nerve-fibers of the cornea, and the fact that the corneal nerves lose their sheaths after penetrating about 1 mm. from the corneoscleral junction, may possibly explain why the lesions never reach the edge of the cornea, but follow only the unprotected course of the nerves. As regards treatment, the general condition should be looked after and a **change of climate** may be necessary. The writer has not seen striking results from **quinine**, but it is nevertheless considered a necessary medication. Postmalarial anemia may call for **iron** and blood examinations may be a valuable aid. Locally, an **antiseptic wash** and **atropine** should be always used and the eye protected. The most striking results will often follow the application of tincture of **iodine**, but this is very painful, even with cocainization and immediate irrigation, and is not always beneficial. **Hot applications** are useful and grateful to the patient. When

the epithelium is regenerated, **yellow oxide ointment** or some similar preparation should be used to lessen the opacity. Refraction should be looked after. E. C. Ellett (Jour. Amer. Med. Assoc., June 30, 1906).

**Mycotic keratitis** is caused by some species of *aspergillus*, commonly *A. fumigatus*, which becomes implanted on the cornea and grows there, the mycelium of the fungus forming a firm mass. This causes a rounded, sharply defined spot of yellowish gray to brown, which may be surrounded by corneal infiltration. There is ulceration beneath the mass, with pain and general evidences of corneal inflammation. The disease runs a slow course until the cause is recognized and the mass scraped away, or until a panophthalmitis develops.

**Dendritic keratitis** is a rare disease also characterized by linear branching ulcers, which tend to extend by the formation of new branches. These branches are usually straight lines meeting each other at definite angles. It may be acute, with severe pain, or chronic, with but a slight irritation.

Galvanocauterization gives good results, but may leave dense scars, which, if the affection is in the center, have serious objections. For the last two years the writer practised a method which avoids these disadvantages. It consists in **scraping of the diseased area** and subsequent painting with **chlorine water**, which proved very successful in 5 cases. Paul Knapp (Klin. Monatsbl. f. Aug., Jan., 1911).

**Herpetic keratitis** occurs late in the acute infectious fevers and in diseases of the air passages. Small vesicles form on the cornea and rupture, giving rise to minute ulcers.

**Punctate Keratitis.**—The term *keratitis punctata* is usually applied to

the small, rounded dots of opacity which form on the posterior surface of the cornea in iritis and cyclitis. Isolated dots of denser opacity in the midst of a somewhat hazy cornea mark a chronic disease of probably syphilitic origin, not attended with much redness or photophobia. Another form called *superficial punctate keratitis*, marked by dots and lines of opacity just below the anterior epithelium of the cornea, is attended with a good deal of conjunctival redness, pain, and lachrymation. It is liable to relapse, and may last for months.

Superficial punctate keratitis (Fuchs) is a form of neuropathic keratitis. The corneal lesions in this condition consist of slowly formed necrotic leucocytic infiltrates seated beneath Bowman's membrane, and are due to the action of pyogenic diffusible toxic substances arising at nerve-terminals. Clinical evidence indicates that the causal nerve-lesion is in the ciliary ganglion, and that it is probably due to the elective action of a systemic toxin on certain of the ganglion-cells therein. There sometimes occurs well-marked focal proliferation of the iris blood-vessels. This observation confirms the view that vascular nevi are neuropathic in origin, and suggests that certain angiomas arising later in life may have a similar origin. Disciform keratitis (Fuchs) is essentially of the same nature as superficial punctate keratitis, and is likewise neuropathic in origin. Traumatic relapsing keratitis is due to a state of irritability in the peripheral ganglion-cells of the corneal nerves resulting from intense stimulation of the nerve-terminals. F. H. Verhoeff (Arch. of Ophthal., Sept., 1911).

*Keratitis punctata superficialis* is a form of corneal affection due to an anomaly in nutrition produced by disturbed secretion of the ovaries. This causes an increased irritability of the vasoconstrictor nerves, and this, again,



brings about an increased diapedesis between the corneal layers. This is shown by the relationship between anesthesia of the cornea and diminution of intraocular tension. The internal ovarian secretion is an important etiological factor of the disease. Bosser (Wien. klin. Rund., Sept. 29, 1912).

**Disciform keratitis** is characterized by a round or oval, sharply limited, gray opacity, situated in the parenchyma of the cornea. The surface over the opacity is somewhat roughened, but rarely ulcerates.

**Filamentous keratitis** is a form in which the proliferating epithelium becomes twisted into minute, thread-like or club-shaped masses, which continue attached to the cornea for a time and may form after a few days again and again over a long period. It may be of traumatic origin, or may be idiopathic.

**Phlyctenular keratitis** occurs commonly in young children, in close association with phlyctenular conjunctivitis. The phlyctenule containing cells and fluid arises on the surface of the cornea, and in a few hours, or a day or two, ruptures and gives rise to a small ulcer. Later a few branching vessels forming a long, narrow leash, usually somewhat in a direction of a radius of the cornea, may make their way out from the nearest portion of the limbus to the region of the ulcer. This is especially likely to occur if several phlyctenules have successively arisen on the same part of the cornea. The condition is then spoken of as *superficial vascular* or *fascicular keratitis*. The ulcers rarely perforate the cornea, but may do so. This form is particularly liable to relapse. It is often attended by the most severe and obstinate photophobia.

**Bullous keratitis** is marked by recurrent attacks of severe burning pain followed quickly by the raising up of a large bleb or bulla on some part of the cornea. The epithelium forming the anterior wall of the bleb quickly ruptures, leaving loose shreds of epithelium and a broad, abraded surface, which in a few days heals over, and some months may pass before there is a recurrence. Two forms of the disease are recognized, one occurring in eyeballs that have been the seat of severe inflammation of the uveal tract, and have undergone degenerative changes; and the other due to previous wounds of the cornea causing extensive loss of the corneal surface in an otherwise healthy eye.

**Pannous Keratitis.**—Pannus is an inflammation and vascular opacity of the cornea, occurring in trachoma, after the palpebral conjunctiva has been severely affected. The portion of the cornea involved is that which comes habitually in contact with the lids; most frequently the upper part, but sometimes also the lower. The part affected is somewhat thickened, with an irregular surface, and more or less hazy. It is usually bounded by a horizontal line marking the habitual position of the lid margin. Large, branching trunks of superficial vessels pass out upon the cornea, from the vessels of the limbus; their distribution is sharply limited by the line bounding the affected area. Ulceration is not infrequent, but is not characteristic of this form of keratitis.

**Traumatic Keratitis.**—Injuries to the cornea may set up a general inflammation of the membrane; but more frequently they cause loss of substance of the cornea, and thus

originate corneal ulcers. If small and not affected, such ulcers heal quickly, with little pain; and leave only a temporary opacity proportioned to their extent. If they involve an extensive surface, even though quite superficial, amounting to little more than an abrasion removing the corneal epithelium, they may be extremely painful. If, as often occurs, they are infected, they present the features of a suppurating ulcer.

**Striate keratitis** is seen after injury, especially after operations, like cataract extraction. In this case a number of fine gray streaks, more or less perpendicular to the corneal incision, are noticed from a few hours to a week or so after the operation. This form may also occur after an injury that has caused bending of the cornea. It usually ends in resolution.

**Suppurative keratitis** always includes the formation of a corneal ulcer, and it is probably always due to some form of infection. The ulcer may be there first, and become infected, or the infection may occur in a previously sound cornea, giving rise to an abscess, which in time breaks through, if not incised, forming the ulcer. In some cases the posterior layers of the cornea break down, forming an ulcer on the posterior surface.

Suppurative ulcer is marked by a margin, which, at least at some points, is infiltrated, or the floor may be infiltrated. The tissue, thus becoming involved in the ulcerative process, is swelled, softened, yellowish in color, and swarming with bacteria. The germs most commonly present are the pus cocci or the pneumococcus (*Diplococcus lanceolatus*). This latter form gives rise to what is known as

the *serpent-ulcer*: an ulcer that is liable to spread irregularly over a large part of the cornea without tending to rapidly perforate it. The margin of such an ulcer is generally of irregular outline, and abrupt or overhanging. The suppurating ulcer is often attended with hypopyon.

**Xerotic keratitis** begins with dryness of the conjunctiva, and a general haziness of the cornea, which soon leads to ulceration, perforation, and loss of the eye. Both eyes are generally affected; the disease occurs in feeble infants, that rarely survive.

Prognosis for life is extremely bad in children in whom keratomalacia develops, breaking down the cornea, in the course of gastrointestinal or other diseases, as it is a disease dependent on the malnutrition of the child. Kapuscinski (Archiv f. Ophthal., Bd. lxxxii, Nu. 2, 1912).

**DIAGNOSIS.**—Keratitis is recognized by careful inspection of the cornea under the proper conditions of illumination. Slight opacity is rendered most evident by strong, oblique illumination, which should be so arranged that the light will be concentrated upon the cornea while the iris behind it is left in comparative shadow, to furnish a dark background. Localized points of opacity in front of the pupil may also be studied with the ophthalmoscope, using the strongest convex lens behind the mirror, and looking from about the focal distance of the lens in front of the eye. Ulceration is best discovered by placing the patient where the light from a large window will be reflected from the surface of the cornea, such a reflex showing all the irregularities of the reflecting surface. To make sure that these irregularities are not filled in with mucus,

that may render them invisible, it is well to wipe the surface with a pledget of cotton. To be positive that the corneal epithelium is absent, or to outline an ulcer more distinctly for treatment, it should be stained with a solution of fluorescein, 1 part; sodium bicarbonate, 2 parts; distilled water, 200 parts; or with one of toluidin blue 1:1000.

Although the great majority of cases of interstitial keratitis are undoubtedly due to inherited syphilis, no syphilitic history is obtainable in at least 30 per cent. of the cases, and in recent years there has been a growing conviction that tuberculosis is responsible for many of these non-syphilitic cases. Hippel, Zimmerman, and others have found tubercular nodules with giant cells in the cornea of suspected cases, and tubercle bacilli, though few in number, have been observed in the giant cells.

In the writer's experience, the projection of a tongue-like area of yellowish-white infiltrate from the limbus into the interstitial lamellæ of the cornea toward its center and the occurrence of discreet, yellowish-white, oval areas, which appear caseous and avascular, are very significant of tubercular keratitis, while he has observed the deposition of small, rounded areas resembling drops of cold mutton fat upon the posterior surface of the cornea or in the lamellæ of the cornea, secondary to tubercle of the iris and of the deeper parts of the eye. According to Michel, the typical picture of tubercular interstitial keratitis is almost always preceded by the formation of tubercular nodules in the pectinate ligament, the corneal involvement appearing secondarily. Bach, however, is of the opinion that tubercular nodules may be found primarily in the periphery of the cornea. William Campbell Posey (*Monthly Cyclopedica*, Sept., 1908).

**Conjunctivitis.**—Keratitis must be distinguished from conjunctivitis. Lesions of the cornea are the most common and the most dreaded com-

plications of conjunctival inflammation. But more especially on that account is it necessary to recognize promptly when the cornea becomes involved. The treatment required by keratitis is, too, in many respects totally different from that appropriate to conjunctivitis. Unless the cornea itself exhibits the characteristic opacity or loss of substance, we cannot assume that it is affected. The redness of the pericorneal zone, while quite different from the typical redness of conjunctivitis, may be completely hidden by swelling of the conjunctiva.

**Iritis.**—The differential diagnosis between keratitis and iritis is also very important. Here, too, the detection of the actual lesions present in one or the other of these structures is to be relied on. Corneal disease may cause apparent discoloration of the iris; and in the early stage of keratitis the pupil is apt to be very small. But the use of a mydriatic (which would generally be very appropriate for either disease) will, in keratitis, produce regular dilatation of the pupil, even if it is not as wide as in the normal eye.

An error, much more grave, is to mistake *inflammatory glaucoma* for keratitis. Both diseases may present pericorneal redness, pain, photophobia, and haziness of the cornea; and glaucoma shows impairment of the sense of touch in the cornea, as markedly as does neuropathic keratitis. In the latter disease the tension of the eyeball may be diminished; in glaucoma simulating keratitis it is always increased. The pupil in glaucoma is more or less dilated; in keratitis, unless a mydriatic has been used, it is contracted or normal. The

haziness of the cornea is more uniform and diffuse in glaucoma, while in keratitis it is more likely to be localized. Corneal ulcer may occur in glaucoma, but usually only in chronic cases. The chief pain of glaucoma is of an aching character, and is felt as much in the brow and cheek as in the eyeball. That of keratitis is more likely to be smarting or burning, or the sense of a foreign body. If a mydriatic has been used and the pupil has been dilated, the tension of the eyeball and the ophthalmoscopic symptoms must be relied on. Haziness of the cornea, sufficient to prevent an ophthalmoscopic diagnosis, is not likely to occur in glaucoma, except when the increase of tension is so great as to be quite unmistakable.

**Diagnosis of Various Forms of Keratitis.**—The diagnosis of the particular form of keratitis present is often very important. Here the character of the opacity or ulceration may be of great significance. Interstitial keratitis will be known by the depth of the opacity, the fine loops of the vessels, the involvement of the iris, and the other evidences of constitutional taint. The history of a nerve lesion or the loss of sensibility in the cornea point to neuropathic keratitis. In the malarial form there is obtainable a history of malaria, and the linear ulcers are in tissue having less than normal sensibility to touch. In dendritic keratitis these features are absent. Herpetic keratitis is characterized by the minuteness of the scattered ulcers and the history of previous illness; and punctate by the points of chief opacity. Bullous keratitis is known by the burning pain, followed by the large bleb or super-

ficial abrasion. Pannus is readily recognized by the distribution of the vessels and the superficial opacity; and the evidence or history of preceding conjunctival disease. Traumatic and striate keratitis will give the history of injury. The suppurative ulcer will be recognized by the yellowish infiltration of the part of the cornea into which it is extending.

#### **ETIOLOGY AND PATHOLOGY.**

—The dominant facts in the pathology of corneal ulcer are that the cornea is a tissue closely related to the white, fibrous connective tissue of other parts, that it is non-vascular, that it is peculiarly predisposed to injury and infection, and that it is covered by epithelium liable to the same injurious influences as the epithelium of the conjunctiva. The tendency of the principal corneal tissue is shown in the controlling influence of the constitutional causes of interstitial keratitis and the prolonged stage of resolution in all forms of inflammation involving the true corneal substance.

The absence of blood-vessels is responsible for the frequent occurrence and disastrous extension of ulcerations, and the danger of the spread of whatever infection may occur. The extension of conjunctival infections of various kinds to the cornea is what might be expected from the similarity of their epithelial coverings.

Traumatism and infection play a part probably in all forms of ulcerative keratitis. Germs are always present in the conjunctiva and atmosphere. So that in the absence of resisting power on the part of the tissues every wound becomes infected. When, however, the germs are markedly pathogenic, as in the

conjunctivitis which attends *chronic lachrymal obstruction*, or in that due to acute infection of the conjunctiva, the corneal lesion proves more serious. Swelling of the conjunctiva around the corneal margin, chemosis, prevents the lids from cleansing the cornea, and produces a sulcus, in which the infected discharges tend to accumulate. It is in this way that chemosis causes corneal involvement in gonorrheal conjunctivitis. The peculiar forms of different ulcers and the way they extend are largely dependent on peculiarities in the growth of the organisms that cause them. Thus, the serpent ulcer, with its rapid extension laterally and its abrupt or overhanging margin, is probably due to the growth of the pneumococcus, which tends to spread between the layers of the cornea without penetrating them.

Ulcers due to the diplobacillus of Morax and Axenfeld are usually small, rounded, and deep, although most of them do not perforate the cornea.

Dendritic ulcer is probably also due to infection. Bullous keratitis may arise from obstruction in the lymph-channels in the part. Pannus is due to traumatism by the roughened lids, probably with an added specific irritant. Xerotic keratitis may be infective, although the so-called xerosis bacillus is found abundantly in the normal conjunctiva. Keratitis may occur in connection with certain diseases of the skin.

Six cases of ulcerovascular keratitis observed following the instillation of tuberculin for the ophthalmic test; 2 more cases—both elderly patients—developed iridocyclitis. These conditions manifested themselves from two to twenty days following the employment

of the Calmette test, as did the reaction itself. The writer thinks it best never to instill the tuberculin until after a thorough examination of both eyes has been conducted. De Lapersonne (*Presse méd.*, Dec. 7, 1907).

Study of 5 cases illustrative of keratitis occurring in connection with rheumatism supplemented by a review of the literature and results of an extensive correspondence with prominent ophthalmologists on this subject. A small majority of correspondents did not report having had such cases occur under their observation. The writer thinks, therefore, that, while the existence of rheumatic keratitis may be considered as established its comparative rarity may be admitted. No special form of keratitis can be called rheumatic, since under various conditions and the changing intensity of the disease it may assume any form. The substantia propria is most frequently affected, as shown by clinical reports. L. Connor (*Jour. Amer. Med. Assoc.*, Aug. 5, 1910).

The rarity of diffuse interstitial keratitis due to syphilitic infection is more apparent than real, because we are apt to overlook the possibility of acquired syphilis in young patients. The writer discusses the symptomatology, and points out that, contrary to the rule in the inherited form, the interstitial keratitis in acquired syphilis almost invariably attacks only one eye. The period of onset varies, within wide limits, from three weeks to twenty-three years. Iritis and vitreous opacities, etc., well forward in the choroid, though not unusual, are far less frequent than in the inherited type. He discusses the pathology, which is naturally somewhat indefinite, since opportunities of microscopic examination in keratitis of acquired syphilis are rare. This condition is a disease of adult life, occurring usually between the ages of 20 and 50, though it has been found in childhood and infancy. Next in etiological importance to syphilis as a cause of interstitial keratitis is tuberculosis. Pflüger has reported 36 cases due to influenza. Interstitial keratitis due to acquired

syphilis responds with remarkable promptitude to antisiphilitic remedies. The local treatment does not differ from that of ordinary interstitial keratitis—**atropine**, **dionin**, and **rest** of the inflamed organ, followed by **massage** with the ointment of the **yellow oxide of mercury**. Carpenter (Annals of Ophthal., Oct., 1908).

Diffuse interstitial keratitis may occur as a result of acquired syphilis. It usually occurs as a late secondary sign of the disease or during relapses in the tertiary stage of the general disease. Stephenson gives the average time of development of interstitial keratitis as 10.8 years after the primary sore. Loewinson has reported one case as early as three weeks after the appearance of a primary sore.

It is difficult to make a clinical diagnosis between the syphilitic and the tuberculous forms of the disease, and even a differential pathological diagnosis is not always conclusive. The prognosis is favorable, though it should be somewhat guarded, from the fact that sight has been lost entirely in one case. A. E. Davis (Jour. Amer. Med. Assoc., July 25, 1908).

Until recently it has been difficult or impossible to explain the latency of the corneal manifestations of inherited syphilis. A child might be apparently in perfect health for five, ten, or fifteen years, and then, perhaps as the result of some trivial injury or slight general illness, develop interstitial keratitis. We now know that the tissues of the syphilitic fetus or baby are literally flooded with the treponema. Such organisms as escape the liver are distributed by the fetal circulation to every part of the body, where (other conditions being favorable) they determine this or that specific lesion. The organisms have been found in practically every syphilitic lesion that has yet been examined with the microscope. Spirochetæ are found, among other parts, in the cornea, iris, and choroid.

It thus appears that, if the child survive, the spirochetæ (possibly in some intermediate morphological form) lie

dormant in the cornea, iris, choroid, and other parts of the eye. They cause no mischief, until some determining cause, of a local or general nature, lowers the resistance of the tissue, and allows the treponema to get the upper hand. This gives rise to interstitial keratitis, iritis, or to choroiditis, as the case may be. S. Stephenson (Ophthalmoscope, Feb., 1909).

Study of 157 cases out of 2223 eye patients observed from 1906 to 1910. Serpent ulcer was most frequent at the time of working in the fields and woods, *i.e.*, between June and August. One hundred and nine stated that the ulcer developed after an injury. Almost constantly the serpent ulcer occurred in eyes previously diseased. One hundred and twenty-nine had an affection of the tear sac and chronic conjunctivitis; 13 had chronic conjunctivitis, blepharoconjunctivitis, or hordeolum. Gunnufsen (Klin. Mon. f. Aug., June, 1912).

The infective agent may persist in one location. Some patients present interstitial keratitis as the only symptom of hereditary syphilis, while others present other symptoms as well. Positive eye symptoms may be present with a negative Wassermann, and the reaction is apt to be absent in the cerebrospinal fluid. The reaction may be made negative by long continued treatment, and the blood be reinfected from the eye. J. A. Fordyce (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., July 7, 1917).

**PROGNOSIS.**—Interstitial keratitis is always slow. In rare cases it may run its course in one or two months; quite as frequently it will require that many years. Until it has fairly begun to subside no one can tell how severe or how protracted the attack will be. If seen early it is pretty safe to predict that the eyes will get worse in spite of all treatment before they will begin to get better; except that in some cases, not all, the early use of salvarsan seems to cut short the

attack. If seen at the height of the attack great improvement may be promised, continuing over a long period. Useful vision will probably be restored even when everything but light perception has been lost. But complete recovery with normal vision rarely, if ever, occurs. If the opacity is most marked at the center of the cornea and many fine vascular loops are seen which extend but a little way on the cornea, the disease is still in an early stage. If the vessels are rather sparsely diffused throughout the cornea, and the opacity chiefly confined to the central region, it is probable that the periphery of the cornea has already cleared, and that the most rapid improvement of vision is about to take place.

For the rarer forms of neuropathic and malarial keratitis the prognosis must depend considerably upon the general condition of the patient. There is some danger of relapses; and it must not be forgotten that ulcers from this disease are liable to infection, with all the consequences thereof. At the best they are likely to leave the affected portion of the cornea nebulous and irregularly astigmatic. Herpetic ulcers, unless greatly neglected, commonly leave no trace. Punctate keratitis usually leaves the cornea slightly damaged; and the syphilitic form is very chronic, with quite incomplete resolution.

Phlyctenular keratitis, if carefully treated, commonly leaves very little permanent damage of the cornea. But, occurring in the children of the ignorant and careless, it is very often neglected; so that a large proportion of the nebulous corneas with high, irregular astigmatism are due to it.

It is extremely liable to relapse; but the single attack yields promptly to treatment, or terminates often within two or three weeks in spontaneous recovery. The tendency to recur is the serious feature of bullous keratitis. But permanent complete recovery may occur in the cases due to traumatism.

Pannus rarely ends in complete recovery. It depends largely on the condition of the lids. If these can be rendered smooth and do not press upon and rub the cornea, it will get comparatively clear, and free from vessels. But some irregular astigmatism always remains. Fortunately the disease does not usually involve the part of the cornea in front of the pupil; so that normal vision may be retained. Striate keratitis usually clears up entirely in a few days or a few weeks. In other forms of traumatic keratitis the prognosis depends on the situation and extent of the loss of substance.

In suppurative keratitis there is always more or less permanent opacity, which is of serious or slight importance according to its situation. The density of the opacity is somewhat proportioned to the depth of the ulcer causing it. The danger of extension in an infected ulcer is indicated by infiltration of its margins or base; that is, by the extent to which the process is invading new tissue. When this extension ceases, when the ulcer becomes "clean," improvement is to be expected. Ulceration is particularly dangerous to the cornea, because it is non-vascular; and when, in the course of an ulcerative keratitis, vessels extend out from the limbus and invade the floor of the ulcer or the tissue immediately around it, the danger of

perforation passes away. Perforation, with prolapse of the iris into the opening, always causes a permanent leucoma, which is serious according to its size and location. (See the section on CORNEA, OPACITIES OF, in the present article.) Suppurative disease of the cornea is often the starting point of an infection that ends in panophthalmitis, or a slower inflammation of the uveal tract, and chronic degenerative changes. And perforating ulcer may ultimately cause sympathetic disease of the other eye.

**TREATMENT.**—While the removal or treatment of the special causes varies with the different forms of keratitis, certain general principles are applicable to the treatment of all kinds of corneal inflammation. In the first place, the general health of the subject has much to do with the resisting power of the cornea, and should be guarded and built up in every way. This does not mean that stimulants should be used in the majority of cases. But it does mean that the patient should have sufficient **nourishing food, fresh air, enough exercise** to keep the circulation and respiration active, **sunlight** and the influences of **cheerful surroundings**, and plenty of **sleep**. To secure sleep it may be necessary to give **analgesics**; but these should be given in **small doses**, and only to supplement the influence of fresh air and exercise. It may be well to give a **laxative**, when needed to promote digestion; but active purgation should be avoided. Tonics, especially **quinine**, may be indicated, and full doses of tincture of the **chloride of iron** seem to have a distinct influence in checking sup-puration.

It is important to remember that we have an infection to deal with, and that constitutional measures are necessary. A brisk **calomel** purge is first given, followed by liberal doses of **quinine**, which can with advantage be combined with **iron and strychnine**. **Atropine**, its strength depending on the severity of the infection, is used. **Holocaine** is very valuable and the constant use of cocaine is condemned. If frequent irrigations with antiseptic solutions and the use of atropine and dionin are not sufficient, pure **carbolic acid** or the **actual cautery** is employed, the former in most cases giving satisfactory results. In virulent types of ulcers, especially those associated with hypopyon, the writer has had brilliant results with subconjunctival injections of **saline solution**, in certain cases injecting from half to a syringe full. The reaction following these injections is insignificant. H. H. McGuire (Va. Med. Semi-Monthly, March 24, 1911).

Local measures must be such as to support, not impair, the vitality of the part. On this account cold applications must be avoided, even where they would be indicated if it were not for the corneal lesion. On the other hand, anything that will keep the eye continuously warm and moist, acting like a poultice, is liable to be injurious. Applications of **hot fomentations for a few minutes at a time**, or the continuous application of **dry heat**, may be beneficial. The danger of its poulticing effect should generally exclude the bandage; but under certain circumstances it may be best to use it. These are: in neuropathic keratitis when the slight traumatism to which the cornea is exposed when the eye is open decidedly aggravate the trouble, and when there has been an injury causing a clean loss of the corneal substance,—an uninfected ulcer. The



**eye should be kept closed**, in any case of corneal ulcer, when exposed to dust that would be likely to lodge in the cavity or be pushed into it by the normal movements of the lids.

Success in treating superficial infiltrations of the cornea with small ulcers by means of applications consisting of an ointment composed of 0.1 Gm. ( $1\frac{1}{2}$  grains) of **ichthyol** and 0.15 Gm. ( $2\frac{1}{4}$  grains) of **cocaine**, in 5 Gm. ( $1\frac{1}{4}$  drams) of excipient. I. I. Federov (Semaine méd., Sept. 24, 1902).

The writer has found that **quinine** is an excellent remedy in a variety of corneal affections not amenable to routine treatment. The sulphate is dissolved in sufficient sulphuric acid to hold the salt in solution. From this is prepared a 1 per cent. solution. The eyes are soaked in this for five minutes four or five times a day, and in addition there is thorough irrigation daily by an undine filled with the solution. It causes little discomfort. A. Lawson (Lancet, Feb. 11, 1905).

Two cases of severe corneal inflammation, one occurring in a man of 23, the other in a boy of 11, which markedly improved under the internal administration and external application of **thyroid gland** after the usual treatment, persisted in for several months, had failed to effect a cure or material benefit. The external application consisted in the instillation of 5 drops (0.3 c.c.) of a 15-grain (1 Gm.) solution three times a day.

Sajous's theory of internal secretions affords an easy explanation of the rapid improvement in the correction of faulty metabolism in structures which need better lymph-supply and a more rapid interchange of the contained nutrient and cleansing fluids. From his experience the writer advocates a smaller dosage than he at first used, having found that from 1 to 2 grains (0.065 to 0.13 Gm.), administered twice or three times daily, would give results equally as good as, if not better

than, larger doses. The early use of the gland in small doses, even where other drugs are properly indicated, prove most beneficial. McCluney Radcliffe (Ophthalmoscope, Sept., 1908).

The writer uses **anaphoresis**. A 10 or 20 per cent. solution of iodide of sodium is painted over the lid, the negative pole is applied to the eye, and the galvanic current passed. Afterward **cataphoresis** may be employed with the positive pole, using **strychnine**. Holt (N. Y. Med. Jour., July 7, 1917).

The results in this disease are proportionate to the severity of the attacks. **Salvarsan** and **mercury** are of great value in treatment in improving the general condition of the patient. **Radium** is of doubtful value. An onset of increased tension indicates a change of treatment locally, and an iridectomy is likely to give good results. Arnold Knapp (N. Y. Med. Jour., July 7, 1917).

In all corneal inflammations cleanliness or **asepsis** is of the highest importance. This is to be secured by **douchings of the conjunctival sac**, and the wiping away of discharges when this is necessary. If there is no conjunctival discharge, washing out the eye once or twice a day may be sufficient. If there is profuse discharge, cleansing the eye every hour may be necessary. The solutions employed should never be irritant; the 2 per cent. **boric acid solution** and the **saline solution** (3 grains to the fluidounce) are the best. They should be applied at **blood-heat** or a little warmer. To wipe away any masses of discharge that accumulate, swabs of absorbent cotton moistened with the cleansing fluid, to prevent the cotton from sticking to the eye, may be used.

Case of a calcareous keratitis in both eyes, a band-like keratitis, a

transverse calcareous film of long standing, at least thirty years. An **iridectomy** had been done, with some improvement. There was no history of previous eye trouble to account for the condition. **Dionin** for one year proved ineffectual; then **sodium chloride**, 5 per cent., was injected, and after the first two or three injections there was considerable improvement, although there is no reason to hope for a permanent improvement. W. F. Coleman (Jour. of Ophthal. and Oto-laryn., July, 1909).

The *pain* of keratitis is commonly lessened by instillations of **atropine** or other mydriatics. It may also be mitigated by brief applications of **very hot water** to the eye, or the internal use of **acetanilide**, **morphine**, or **codeine** in small doses. It is temporarily relieved by **cocaine**. But this should never be prescribed, because the after-effects are altogether bad; and the temporary relief it affords tempts the patient to frequently repeat the applications, each of which aggravates the disease. **Holocaine** is less likely to be harmful when used in this way, and it has a decidedly antiseptic action. In non-suppurative keratitis with severe neuralgic pain it may be used in 1 per cent. solution every two hours. The best cure for pain is, in general, the cure of the condition causing it. It is in this way that **physostigmine** (eserine) quickly relieves the chronic, very painful, shallow ulcers that occur at the margin of the cornea in elderly people with chronic catarrhal conjunctivitis.

**Photophobia** may be lessened by the wearing of **dark glasses only when exposed to strong sunlight**, or light shining on water or snow, and the avoidance of sudden changes to a bright light. But it grows rapidly

worse if dark glasses are worn all the time, or the patient be confined to a dark room; and the confinement is likely to react unfavorably on his general physical condition. Of course, during an active keratitis the eyes should, as far as possible, be allowed to **rest**.

**Special Treatment.**—*Parenchymatous* or *interstitial* keratitis especially requires the employment of mydriatics on account of the tendency to involvement of the iris. **Atropine** may be used in solution of: atropine sulphate, 1; distilled water, 60. The frequency and freedom of its applications may be limited by the tendency to cause mydriatic intoxication. When sufficient to keep the pupil well dilated, the strength of the solution and the frequency of its application may be diminished.

In a severe case of interstitial keratitis the right eye had been inflamed and painful for three months, with severe pain. Very marked **interstitial corneal changes** were present, especially over the lower half, with superficial pebbling, which stained very slightly. Under atropine the pupil was found to dilate irregularly because of posterior synechiæ. The only treatment prescribed was a 5 per cent. **dionin** salve. The results were striking. The cornea largely retained its luster, was no longer roughened, and the interstitial changes were clearing. Melville Block (Jour. of Ophthal. and Oto-laryn., June, 1908).

Locally, **hot fomentations**, and sometimes **local bleeding** from the temple, may also be employed. But the curative treatment is probably chiefly constitutional: first, the preservation of the general health and, after that, the prolonged administration of **mercury** and the **iodides** in moderate doses. **Codliver oil**, **iron**,

and arsenic are sometimes most beneficial. **Salvarsan** generally diminishes the photophobia and irritability of parenchymatous keratitis due to inherited syphilis, and in some cases, used early, it is of great benefit. For this purpose it should be given in full dose, repeated two or three times at rather short intervals. It has more influence in cutting short the inflammation than in removing the opacity.

In the treatment of tubercular keratitis, some form of **tuberculin** is a most important remedy.



Nebulous corneal haze. Sequela of tubercular deposits on Descemet's membrane as shown in colored plate.

Personal case of keratitis tuberculosa relieved by **tuberculin** injections. Von Hippel reports 2 cases, 1 of chronic inflammation of the cornea and lids, and another of eczematous disease of the cornea, each relieved by a few injections of tuberculin. In 1904 he reported 2 other cases of corneal nodes cured by tuberculin injections. Cohn (1891) used three injections in 2 cases of interstitial keratitis associated with phlyctenular lesions. Kocnigshofer and Maschke (1891) report a case of interstitial keratitis cleared up in six days by two injections of  $\frac{1}{2}$  mg. Uhthoff (1891) reports a case of vascular keratitis resembling interstitial, which responded to  $\frac{1}{1000}$ -mg. injections of tuberculin. Gradle (1900) refers to 4 cases of atypical scrofulous keratitis which responded to tuberculin injections.

Schieck (1900) reports a mixed case of iris and corneal nodes which yielded to twenty-four injections of tuberculin, but strangely without reaction. Morax and Chailous (1901) report 2 cases of corneal nodes absorbed after one injection of tuberculin which gave both local and general reaction. Enslin (1902) records 8 cases of supposed interstitial keratitis with typical reaction after injections of  $\frac{1}{10}$  to 3 mg. of tuberculin. He differentiates in this way between syphilis and tubercle. Out of 24 cases tested, 5 gave the typical reaction. Darier (1903) has used tuberculin in a case of supposed interstitial keratitis with marked reaction and curative results. Stan-  
culeano (1904) reports 5 cases of typical reaction in corneal infiltration with and without iritic lesions. Gamble and Brown's (1905) case was one of iritic nodes, but with pinhead-sized, thin, yellowish-white masses deposited on Descemet's membrane, which make this a corneal case. The lesion was relieved by repeated tuberculin injections.

The following points are emphasized: 1. Keratitis tuberculosa closely resembles interstitial keratitis in its clinical manifestations (see *colored plate*). 2. The use of tuberculin injections is our most efficient method of making a differential diagnosis. 3. Confirmatory evidence should be gathered from bacteriological examinations, inoculation tests, and the study of systemic signs. 4. Tuberculin injections have an undoubted therapeutic value in tuberculous lesions of the eye. 5. Two minims (0.12 c.c.) of Koch's tuberculin (Mulford) are sufficient for a diagnostic test, while from 2 to 5 minims (0.12 to 0.3 c.c.) may be injected for therapeutic effects. S. Lewis Ziegler (Ophthalmology, April, 1907).

Nothing is nearly so efficient as **salvarsan** in the treatment of interstitial keratitis. Although cure with mercury is beyond a doubt, a longer time is necessary, during which connective tissue would have been de-



Keratitis Tuberculosa. (*Ziegler.*)  
Ophthalmology.



posited in the cornea, and the ultimate vision have been much worse. Salvarsan works so quickly that connective tissue has not time to form. In the writer's cases, also, the corneal infiltrate, even after subsidence of inflammatory symptoms, has been absorbed to a much greater degree than with mercury. Salvarsan will not cause the disappearance of the old scars of a past interstitial keratitis, but if used when the least trace of acute symptoms is present it will check the inflammation, absorb the infiltrate, and prevent further deposit of connective tissue. G. W. Vandegrift (Med. Record, Oct. 26, 1912).

For *neuropathic, malarial, and herpetic keratitis*, the general and tonic treatment is of most importance, with careful protection of the eyes from irritants.

The treatment recommended to prevent *keratitis after destruction* or removal of the *Gasserian ganglion* is: stitching the lids together for the first few days, and, after the removal of the dressings, keeping the eye covered with a Buller shield for a month. For *punctate keratitis atropine* should be applied.

*Bullous keratitis* may be met with *atropine* and hot applications during the attack, and regular *massage* with some mild ointment during the intervals. It may also become an indication for the *enucleation* of a degenerated eye.

The writer has been advocating for nearly thirty years vigorous *massage* of the *eyeball* applied for fifteen minutes ten or fifteen times a day, lubricating with a little salve, to enable the eyelids to slide easily over the eyeball. In this manner he has been able to cure parenchymatous keratitis in seventy days unless there were pronounced Hutchinson teeth, in which cases the course required from ninety to a hundred days to accomplish the same results. If the leuco-

cytes that have invaded the cornea in such quantities are left in peace, there is more or less blindness for months or years. But if, with vigorous, constantly repeated *massage*, the leucocytes are kept stirred up and mobilized, they are easily swept along by the circulating blood and the *massage* aids in developing the blood-vessels that flush out the leucocytes. During the entire course of treatment he keeps the pupil dilated with *atropine* to prevent any complications on the part of the iris, especially posterior synechia. The course may be completed or hastened by a few conjunctival injections of a 1 or 2 per cent. *salt solution*. Grandclément (Lyon méd., June 18, 1911).

*Dendritic ulcer* should be *scraped* and touched with a solution of *silver nitrate* or *formaldehyde* of a strength of 1 to 60.

*Phlyctenular keratitis* was long known as the common form of scrofulous ophthalmia, and must be treated with especial reference to the general conditions that accompany it. *Outdoor life*; plain diet; readily digested food and the avoidance of sweets, tea, and coffee must be insisted on. *Cod-liver oil* and syrup of *iodide of iron* are standard remedies. The child must not be allowed to keep the eye buried in the pillow or handkerchief, but should be encouraged to *overcome photophobia* by exposure to the light and air. Local treatment is also very important. Photophobia will be diminished by the instillation of *atropine*. The *ointment of yellow oxide of mercury*, 1 part; petrolatum, 60 to 120 parts, should be used in the conjunctival sac every night. The lower lid being drawn down, a piece of the ointment the size of a grain of rice is placed on its inner surface, and the lids are closed and then rubbed gently over the eyeball for a minute or two.

If there is much redness of the ocular conjunctiva or enlargement of the veins on the inner surface of the lids **tannin, 1; glycerin, 60**, should be applied to the everted lids every day or two.

Treatment should be continued many weeks after an attack to prevent recurrences. A most important measure for the same purpose is the thorough eradication of all morbid conditions discoverable in the nose.

For chronic ulcers that show little tendency to become covered with epithelium trial should be made of **scarlet red**, in an ointment containing from 1 to 5 per cent. of that drug, which may be applied freely within the conjunctival sac, two or more times daily.

In hypopyon keratitis, if the ulcer be pneumococcal, the sooner recourse is had to surgical interference the better. Should there be dacryocystitis, **ligature or cauterization of the canaliculi**, after flushing the sac freely with physiological **salt solution**, should be done without delay.

If the condition turns out to be diplobacillary, cauterization is not only unnecessary, but injurious. The diplobacillus succumbs readily to **zinc preparations**, such as sulphate of zinc solution, 2 grains (0.13 Gm.) to the ounce (30 Gm.), instilled freely into the eye as often as every hour in bad cases. It is applied, to begin with, under pressure such as can be got with an Anel lachrymal syringe or a hypodermic syringe. **Atropine drops, ½ per cent.**, are also instilled to break down adhesions and rest the eye, and **hot fomentations** in severe cases.

If this simple method of treatment be carried out thoroughly it is most satisfactory. The diplobacilli disappear altogether in a few days from the eye, and regression of the ulcer quickly sets in. MacGillivray (Edinburgh Med. Jour., July, 1909).

In cases of *ulcus serpens* due to the diplobacillus of Morax-Axenfeld the treatment with **zinc sulphate** was found very efficacious. Other methods of treatment were tried. Gabrielidis and Morax instilled **sterile bile** and solutions of **cholic acids**. **Phototherapy** and **bovine serum** were also used, but with very little effect. As for **curettage** with a sharp spoon, opinions differ. Some consider it injurious, owing to the danger of producing infection; others consider it of great benefit in suitable cases. R. Schneider (Wiener klin. Rundschau, June 5, 1910).

The writers maintain that **iontophoresis with zinc ions** is an extremely efficient procedure in the treatment of septic ulcers of the cornea, seeming to surpass all other methods employed up to the present time, especially when used in conjunction with **paracentesis of the anterior chamber**. Labowski and Sachs-Mulke (Med. Klinik, Feb. 5, 1911).

*Pannus* requires the thorough treatment of the morbid conditions of the lids which cause it, sometimes including canthoplasty, or other operations on the lids to relieve the cornea from abnormal pressure. Other special measures for the treatment of opacity are mentioned in the following section:—

*Suppurative keratitis* requires the prompt and **thorough removal of infective discharges and infected tissue** so far as possible. Corneal **abscess** should be freely **opened** as soon as it is recognized. For infected ulcers the simplest and most generally applicable treatment is **scraping** or **curetting**. The tissue around the ulcer should be thoroughly and repeatedly scraped toward the ulcer so as to empty the interlamellar spaces of their contents; and all softened tissue should be removed. After

scraping, the ulcer should be closely watched; and upon any evidence of farther extension of the infective process thoroughly scraped again.

For small ulcers, after carefully cleaning the surface, one of the best means of checking farther extension is by the application of **nitric acid**. This may be used pure or diluted with an equal quantity of water in this manner. A smooth wooden toothpick or matchstick is dipped into the acid, and then held in the air *until all the acid is absorbed into the wood, so that the surface no longer appears shiny*. The wood is then pressed against the surface to be cauterized, which quickly turns white. This can be repeated after a day or two if necessary.

The writer has treated over 200 cases of corneal ulceration, both of the phlyctenular variety and those of traumatic origin; and while at first it was his custom to resort to **iodine** in all simulating conditions, an experience of five years has led him to the conclusion that its special adaptability is to ulcers that are indolent in type. It lessens rather than increases scar-tissue. For the latter it seems to possess a peculiar affinity and to exert a remarkable influence. The after-treatment should vary according to the indications of each individual case. The judicious use of iodine cannot be too warmly advocated; and while, in some instances, two and even three applications have been necessary to effect a cure, the majority of cases have readily yielded after its first employment.

Preference should be given to the **tincture of iodine**. The eye should be first cocaineized to complete anesthesia. This having been accomplished, an eye speculum is introduced and the ulcer scraped thoroughly with a spud or equally convenient instrument. The part is then dried well, and with a few fibers of absorbent

cotton twisted tightly around an ordinary wooden toothpick, small probe, or applicator, previously immersed in the undiluted medicament, the iodine is applied thoroughly to the ulcer. Care should be taken, however, to dry off the excess, and none of the drug should be allowed to come in direct contact with the healthy parts of the eye. The organ should be subsequently bathed with sterilized water or **boric solution**, and then treated as a recent traumatism of the cornea. J. Lawton Hiers (Phila. Med. Jour., Nov. 29, 1902).

Case of multiple corneal ulcers in a young man with a history of epiphora of several years' standing who, in the week before, had developed one large and eleven very small superficial ulcers of the cornea of one eye, following influenza. Iodized phenol was of no apparent benefit, but applications of **nitric acid** were effective. **Protonuclein** had been dusted in once that day. The globe was still very red and the eye painful, but the corneal epithelium took scarcely any stain from fluorescein. E. R. Neepser (Jour. of Ophthal. and Oto-laryn., June, 1911).

The writer recommends a watery solution of **iodine**, 1 grain (0.065 Gm.); **sodium iodide**, 3 grains (0.2 Gm.), and water, 1 ounce (30 Gm.), in the treatment of corneal ulcer. Three drops (0.18 c.c.) of this solution, instilled into the eye three or four times daily without other treatment, has been, in his hands, very successful. The application is not very painful, and the pain lasts only ten or fifteen minutes. Occasionally the conjunctiva becomes congested during the treatment, but this is only temporary. After twenty-four or forty-eight hours the eye becomes less painful and more tolerant to light, and the headache, common in these cases, rapidly diminishes. The solution can be used for several weeks without causing further annoyance, even if the ulcer is healed. The writer has treated 15 cases by this method with encouraging results.



E. L. Meierhof (Jour. Amer. Med. Assoc., Aug. 26, 1911).

Equally as efficient as scraping, though a little more alarming to the patient, is the application of the **actual cautery**. This application may be made with the galvanocautery tip; or with a piece of steel knitting-needle, one end of which is held in an alcohol flame until white hot, and then quickly applied to the affected portions of the cornea. The cauterization should include all infected parts of the tissue. After cauterization the eye may remain undisturbed for a day or more except that it must be kept cleansed.

Among the preparations which have been recommended in recent years for the treatment of ulcerative keratitis have been various **sera**, none of which, however, seems to have merited the claims originally made for them, though useful in a certain proportion of cases.

Fully 95 per cent. of all corneal ulcers are the work of the pneumococcus. The writer has consequently been treating such ulcers with **anti-pneumococcus serum**, and found that the majority of the patients were promptly cured. In 20 cases of suppurative keratitis with hypopyon, 16 were cured, 1 showed no improvement, and 3 did not return to finish the course of treatment. The results were less favorable in 3 cases with multiple foci, in which the affection continued its course to loss of vision in all but 1 case. The serum was injected under the conjunctiva, and also instilled every four hours, supplemented by the usual measures. Castresana (Siglo Medico, vol. lli, No. 2668, 1905).

Twenty-one cases of *ulcus serpens* corneae were treated by the writer with the **pneumococcus serum**, recently recommended by Roemer. In the majority of cases pneumococci

were found in the secretion from the affected eye. Some cases were treated with the serum alone; in others the serum was injected together with an emulsion of the dead bacilli, while in still others **galvanocautery** was also employed. The injections were always given into the skin of the back, and a reaction was never seen. On the whole, the results were very favorable. D. Wanner (Wuertt. med. Correspbl., 1905; Merck's Archives, Nov., 1905).

Promptness is necessary in treating ulcer of the cornea, as many eyes are still lost every year from progressing hypopyon keratitis. **Anti-pneumococcus serum** is a valuable adjuvant, but cannot be relied on exclusively. The writer recommends applying the **galvanocautery**, even in the very earliest stages, using it at a low red heat, so as not to destroy the sound cornea beneath in the incipient cases, supplementing it with perforation and cleansing out the ulcer excavation in severe cases. **Boric acid** or **sublimate salve** afterward is more effectual than iodoform. Helbron (Berl. klin. Woch., Bd. xliii, No. 21, 1906).

The serum therapy of pneumococcus ulcer of the cornea is not yet out of its experimental stage, and the clinician is not to be blamed if he still gives preference to other proved therapeutic resources. Schneider (Münch. med. Woch., May 10, 1910).

Large doses of **pneumococcus serum** brought about prompt cure in 70 per cent. of cases of pneumococcal corneal ulceration. Gebb (Deut. med. Woch., Dec. 7, 1911).

Case of keratitis in which a smear taken from the cornea of the inflamed eye made it evident that the ocular inflammation was due to gonococci, these organisms being present in large numbers. Gonococci were also found in the secretion from the urethra. Although the patient confessed that there had been more or less discharge from his urethra during the greater part of twelve years.

he had never suffered from rheumatism or other painful affections of the joints or body. The patient was admitted to the hospital, and was treated locally by **heat, atropine, iodoform**, and later by **dionin**, and generally by injections of **antigonococcic serum** into the buttock, in doses of  $\frac{1}{2}$  to 1 c.c. (8 to 16 minims).

At no time could the serum injections be said to have favorably influenced the inflammation of the eye. Considerable febrile reaction resulted from the injections, upon a number of occasions the temperature rising to 100° and a fraction Fahrenheit (37.8° C.), but it was impossible to definitely determine whether a local reaction in the eye followed or not, as the eye continued to be very actively inflamed for six weeks or more, all forms of local treatment making but little impression upon it. The injections of the serum seemed, however, to exercise some favorable influence upon the urethritis, as the discharge gradually lessened after a few had been administered, although this result may also have been obtained by rest in bed and attention to diet. Wm. Campbell Posey (Ophthalmic Record, May, 1909).

In *acute staphyloma*, or protrusion of the cornea or sclera, a complication often encountered in ulcerative keratitis which greatly compromises vision, instillations of a 1:1000 solution of **epinephrin** three times daily have been recommended.

In corneal ulcer there are a hyperemia of the conjunctiva and an albuminous exudate into the anterior chamber. Any remedy which will contract the blood-vessels will lower the tension and restore the condition of the cornea by freeing the lymph-spaces. These indications are all met by **adrenal extract**. Three cases treated by the writer were rapidly cured by applications of adrenal extract and **chloretone**. In one case there were several relapses until a 5 per cent. solution of **nuclein** was added

to the treatment, when the tendency to recurrence ceased. W. L. Phillips (N. Y. Med. Jour., Oct. 3, 1903).

**Epinephrin** in acute staphyloma of the cornea. Experimentally it has been found to reduce the formation of the aqueous humor in animals, and a close observer has reported one case of double glaucoma in which the solution not only relieved the pain, but caused some contraction of the pupil. Sajous pointed out that the influence of adrenal extractives was due to the great rise of a metabolic activity it engenders directly in the muscular elements of the arterioles, including those which supply the cornea and the sclera. The caliber of the arterioles being reduced by the contraction of their muscular coat, the volume of blood-plasma admitted to the ocular structures is also greatly reduced. The veins which carry off the blood from these structures are not influenced, however, and the intraocular tension is relieved, merely because more fluid leaves the eye than is supplied by the arterioles. On account of this physiological action, the writer was induced to try epinephrin in several cases of acute staphyloma of the cornea, so frequently seen in ulcerative keratitis, instead of puncture and pressure bandage, or later doing a partial excision of the cornea. A 1:1000 solution of epinephrin was instilled three times daily. This caused the bulging gradually to disappear, sometimes quite rapidly. No failure occurred when the solution had been used as directed. P. J. Pontius (N. Y. Med. Jour., Sept. 28, 1912).

A powerful agency for draining the affected tissue, and establishing lymph-currents that shall check the progress of infection, is the **Saemisch incision**, made by thrusting a narrow cataract knife beneath the ulcer, letting it cut directly out, dividing all the affected tissues, and permitting the free drainage of fluid from the anterior chamber. This incision may

be made at the lower margin of the cornea, where it seems as effective as if made through the ulcer. It is often well to reopen it with a blunt instrument each day until improvement is well started.

### INJURIES OF THE CORNEA.

**BURNS**, either by heat, acids, or caustics, may cause corneal ulcers and permanent irregularity of curvature or opacity. A burn by heat or by nitric acid may cause a superficial coagulation of the corneal tissue, giving an impression of complete opacity of the membrane; but upon the separation of the injured tissue, which may occur in a few hours, or at most a few days, the cornea is found to be clear and comparatively uninjured. Burns by lime are frequent, and very serious in their effects, the lime forming a union with the tissue, which makes it difficult to remove, and continuing, therefore, to act as a caustic for a considerable length of time.

**Treatment.** — Simple burns by steam or hot metal, after removal of the metal, should be treated by keeping the eyes closed under a light **bandage** and cleansing twice a day with **boric acid solution**.

Injury by quicklime may be met by the filling of the eye with **olive oil**, and especially requires the earliest possible removal of all the retained caustic. Other caustic alkalies may be neutralized by very dilute acids, as **vinegar and water**; but reliance should be mainly placed on washing with water or solution of **boric acid**.

Acids may be neutralized by lime water, or solutions of **sodium** or **potassium bicarbonate**, or **soapsuds**. But the best means is by free washing of the conjunctiva with a 1 per cent. solution of **sodium bicarbonate**.

**FOREIGN BODIES** are so frequently imbedded in the cornea because the cornea occupies nearly two-thirds of the space between the opened eyelids, and a much larger proportion of that space when the eyes are partly closed, as they are when the entrance of a foreign body is anticipated. Again, the tissue of the cornea is of such consistence as to retain such particles as may penetrate it, whereas the conjunctiva and subconjunctival tissue are so loose that foreign bodies imbedded in them easily work out.

When a foreign body is imbedded in the cornea it commonly causes irritation and suppurative inflammation, by which it becomes loosened and easily drops out, or is wiped away by the lids. If, however, it lies at the bottom of a considerable loss of substance it may lie there for some time, although quite detached from the corneal tissue. Under these circumstances it becomes a source of irritation, causing chronic weakness of the eye, photophobia, and excessive lachrymation, and the development of vessels in the adjoining part of the pericorneal space, which push out to the seat of the foreign body, giving an appearance of a chronic phlyctenular ulcer or superficial vascular keratitis.

**Diagnosis.**—The search for a foreign body in the cornea should be made by all the following methods:

As to examination, oblique illumination, using the ophthalmoscope, and with the eye placed so as to reflect from its surface an area of light, as before a large window. If the foreign body has been imbedded many hours or days there also will be pericorneal redness, most decided at the part of the corneal margin nearest the foreign body. In using oblique illumination foreign bodies of light color are rendered evi-

dent when the light is strongly concentrated on the cornea and the iris in comparative shadow. Dark particles are rendered distinct by concentrating the light on the iris behind, thus furnishing a light background. Light foreign bodies are best seen against the black pupil; dark ones against the illuminated iris. It is, therefore, necessary to vary the oblique illumination and to look at the cornea from different directions.

With the ophthalmoscope all opaque foreign bodies appear black against the red reflex from the pupil. By turning the eye in different directions, this reflex must be obtained through different parts of the cornea. Sometimes with the ophthalmoscope the appearance of a foreign body is caused by a slight disturbance of the corneal surface; so that after the position of such a black speck has been ascertained it must be examined by oblique illumination.

The reflection of an area of light, as a large window opening to the sky, or a strongly illuminated card held close before the eye, is uniform from the normal cornea. But when, by the presence of a foreign body, the corneal surface is roughened, the irregularity caused in the reflection is very noticeable, and furnishes the most readily applicable method of recognizing the presence and location of such an injury or foreign body. If, however, the disturbance of the surface be slight, it is liable to be masked by the layer of mucus which covers the normal cornea, and to avoid this source of error the corneal surface should be dried by touching it with a bit of absorbent cotton. By using a solution of fluorescein, as for corneal ulcers, one may succeed in staining a small area, which shows where the foreign body is, and furnishes a background against which it is more distinctly seen.

The writer has seen hundreds of cases where injured men have gone to a surgeon to have a foreign body removed from the cornea where the cornea had been scraped and damaged in such a manner as easily to invite infection. Such infection had actually occurred in many instances, and in not a few cases the eyes have been irretrievably damaged or lost by dirty and careless efforts at the removal of corneal foreign bodies.

In most shops will be found some workman who is supposed to be especially qualified for this kind of work. He keeps a magnifying glass and some kind of an instrument of more or less improper quality and usually dirty at his bench, and is sometimes kept quite busy in his efforts at removing foreign bodies from the cornea. Some of these men use a few drops of cocaine, which, of course, renders the operation very much easier, but most of them do not use any local anesthetic, under which circumstances, of course, the eye is in constant motion, and before the operation is finished the cornea is badly scratched and abraded by the awkward manipulations of the "shop oculist." Frank Allport (Railway Surg. Jour., April, 1912).

**Treatment.**—In general, foreign bodies lodged in the cornea should be at once **removed**. This is usually a very simple operation, with the eye placed under the influence of local anesthesia. A single drop of a 2 per cent. solution of **cocaine**, or a 1 per cent. solution of **holocaine** placed directly upon the cornea produces the necessary anesthesia in from three to five minutes. Occasionally a foreign body can be wiped away by a little absorbent cotton wrapped closely and firmly around the end of a probe or matchstick. If more firmly imbedded the ordinary **spud** is to be used by thrusting it into the wound alongside of the foreign body, and by something of a

wedge-like action, pushing the foreign body out.

Foreign bodies of a certain character, as splinters of wood or the beards of grain or grasses, may require to be extracted as a splinter is extracted from the skin, by making an incision along it with a needle or cornea knife, so as to freely expose it, and then lifting it out of its bed. When the foreign body extends somewhat into the anterior chamber, the eye should be kept quiet until the aqueous humor has refilled the chamber. Then a broad needle is to be thrust underneath the foreign body, and held with its point imbedded in the posterior surface of the cornea while the foreign body is extracted.

Occasionally when the condition of the patient, or the lack of proper instruments, or of a local anesthetic renders the extraction of the foreign body impossible, it is proper to cleanse the surface of the eye as thoroughly as possible, and allow it to remain for a few days until the process of suppuration has loosened it. Then it can be washed or wiped out. But such a process is always attended with danger of infection of the deeper structures of the eye and serious damage or complete functional loss of the organ.

Bits of iron imbedded in the cornea very quickly give rise to a brown stain, probably due to oxide of iron. This stain may remain after the removal of the foreign body, but it is always cast off within a few days. It is better to remove it at once by scraping, as it often proves a source of irritation and always ultimately separates as a slough.

Powder grains imbedded in the cornea at first cause much irritation and inflammation. But if this has passed away the remaining stain, consisting of minute particles of carbon, may be retained

indefinitely, without being a source of further trouble or danger.

**CORNEA, OPACITIES OF.**—The bulk of the cornea, being a highly specialized tissue closely related to ordinary connective tissue like that composing the sclera, is liable by slight degeneration to lose its transparency. All considerable injuries or losses of substance of the cornea are repaired by cicatricial connective tissue, which usually fails to become entirely transparent. Hence, corneal opacities are a probable sequel of all other diseases or injuries of the cornea. Slight haziness of the cornea is spoken of as *nebula*. A more dense localized haziness, amounting to almost complete opacity, is called a *macula*. More dense and complete opacity, from its usual color, white, is called *leucoma*. The density of the opacity indicates the severity of the lesion causing it; but recovery from severe lesions is more complete in early life.

Case of dystrophia epithelialis corneæ (Fuchs) observed ten years in a man aged 70, of normal physical and mental conditions. The disorder commenced with a gray, transverse, oval opacity, 4 by 2.5 mm., in the lower portion of the cornea, extending to the middle of the pupil, with a more opaque, grayish-white seam and uneven surface. The loupe showed in the opacity very fine, black dots, which proved to be gaps of tissue. Pupillary reaction, tension, sensibility of cornea, and fundus were normal. V. R. with —4.00 4.12. 1. 4.8. After two months vesicles developed at the center of the opacity under slight subjective sensations, burning and feeling of a foreign body, which soon subsided. In the course of years these conditions developed and disappeared, later with streaky opacities, insensibility of the cornea; pain in eye, forehead, and vertex; then with development of blood-vessels in the shape of fas-

cicles, swelling of the conjunctiva, increase of the opacity in density, and ectasia of the cornea. Then the left eye was affected and showed the same course. The eyeball assumed a yellowish-gray coloration, under almost complete disappearance of the superficial blood-vessels, dull luster of the conjunctiva, and diminished sensibility. The pupils were narrow and had very little tendency to respond to mydriatics. The treatment alleviated the subjective symptoms only temporarily. Characteristic was the great chronicity of the affection, about fifteen years to the full development of the right eye. J. Coelin Hoppe (Klin. Mon. f. Aug., Feb., 1912).

*Congenital opacity* of the cornea is rare. It may arise from intra-uterine inflammation, or from an arrest of the normal clearing of the cornea, which is originally opaque. This clearing beginning at the corneal margin, such opacities usually involve the center. They may diminish in early childhood, although this is unusual, and occasionally somewhat similar opacities are said to occur after birth and to increase.

*Family opacity of cornea* appears usually about puberty, but may be first noticed much later in life. Dimness of vision calls attention to the eye, and the cornea is found to contain opacities, either interlacing lines (lattice-form or grill-like) or nodules, dots, and circles (the nodular opacity). It is most pronounced near the center of the cornea, but gradually extends toward the periphery, preventing any useful vision. There is no inflammation. The condition is hereditary. No treatment is known to be of benefit, except **iridectomy** when the natural pupil is covered by the opacity.

**Varieties.**—The opacity usually occurring with age as a gray arc slightly within the upper and lower margins of

the cornea is the *arcus senilis*. It extends in some persons to form a complete ring, *annulus senilis*, separated by a zone of comparatively clear cornea from the sclera. Sometimes it occurs in early life, and even in early childhood. Sometimes an opacity resembling *arcus senilis* is attended with thinning of the cornea, *peripheral groove formation*, and this causes bulging of the cornea and high, irregular astigmatism.

*Opacities due to inflammation* of the cornea are most dense immediately after the subsidence of the inflammation, from which time they diminish with greater or less rapidity according to the age of the patient and the nature of the opacity. Sometimes quite a noticeable macula will be left by an inflammation occurring a few weeks previously that has been quite overlooked or forgotten. The general clouding of the cornea from interstitial keratitis clears first from the margin, and, usually in the course of several months, or one or two years, is reduced to a nebula, although perfect recovery is rare.

Case of syphilitic opacities of the cornea in a lad of 17 who was the subject of congenital syphilis. During an attack of interstitial keratitis there appeared a triangular opacity in the superficial layers of the cornea, which had to be differentiated from certain forms of keratitis parenchymatosa. The opacity was entirely avascular and was composed apparently of a series of fine lines, which ran in a generally vertical direction from the base to the apex of the triangle. The rest of the cornea presented the general diffuse haze and remnants of interstitial vessels which are usual after interstitial keratitis. W. C. Posey (Ophthalmic Record, Feb., 1906).

Opacities connected with anterior synechia, adherent leucoma, remain dense throughout life. Vascular opaci-

ties connected with granular or phlyctenular conjunctivitis, are capable of great improvement after the cure of the conjunctival diseases that cause them. Those due to granular conjunctivitis, or trachoma, commonly involve the upper half of the cornea, the part in contact with the roughened upper lid, and sometimes encroach slightly on the lower margin, where it comes in contact with the lower lid. Those due to phlyctenular keratitis take the form of a fasciculus of vessels running out from one or more parts of the corneal margin.

Case of corneal opacity following cataract extraction, the first in the writer's experience of 209 cataract operations. Opacity had already existed in the other eye (left), which had been operated on ten years before. This was probably due to bichloride of mercury, as that antiseptic was much used at the time, but no such cause existed for the opacity in his operation. In view of the lack of literature on the subject, the writer addressed a series of questions to the members of the Section on Ophthalmology of the American Medical Association, asking their experience with such cases. Out of the 227 heard from at time of writing, 87 gave either the exact or estimated number of extractions, amounting to 19,821. From the figures given, a conservative estimate of the extractions by his correspondents would not be less than 50,000, and among these there were only 39 cases of general opacification. V. H. Hulen (Jour. Amer. Med. Assoc., July 25, 1908).

Anterior, or *corneal*, *staphyloma* is the bulging opacity which follows perforation of the cornea, either by traumatism or by ulcerative inflammation, leading to prolapse of the iris and union of the iris and new-formed tissue in the corneal scar. It does not necessarily ensue in all cases of prolapse of the iris into a corneal opening. After cataract

extraction very extensive prolapse of the iris may occur, and yet, without any active treatment, the prolapse will in time entirely flatten down, leaving a slight opacity with adhesion of the iris at the side of the corneal incision. The same favorable termination is also seen in cases of traumatic perforation other than operative, and sometimes in perforation due to small ulcers. The determining factor as to the occurrence of staphyloma appears to be the general condition of the cornea, and possibly of the iris, that becomes adherent to it. If these are the seat of extensive inflammatory changes, there is strong probability of increasing bulging of the cicatrix.

In young children the general adhesion of the iris to the cornea is followed by bulging of the whole cornea and even great enlargement of the eyeball; in older persons staphylomata are likely to be more strictly localized, and, if the bulging is great, they rupture.

Opacity following the use of a lead lotion upon an ulcerated cornea has long been recognized and ascribed to the deposit of metallic lead in the denuded corneal tissue. But this explanation is now shown to be incorrect, for at least some of these cases. Corneal opacity may also follow applications of silver nitrate, when it is brown or dark, or after use of copper sulphate when it is greenish.

Opacity from *pigment deposit* in the cornea is of two kinds. In one, small spots of black or brown pigment are deposited in the cornea, late in the history of an intraocular inflammation which has usually been attended with high tension. Such pigment deposits are likely to be permanent. A temporary general staining of the cornea by blood-pigment occurs after extensive hemor-

rhage within the eyeball. The staining is at first comparatively uniform, and clears up from the margin of the cornea. A greenish staining of the cornea is sometimes seen in connection with multiple sclerosis, or pseudosclerosis.

Two additional cases to the 2 cases previously reported from the Tübingen clinic by Kayser in which a nervous affection resembling multiple sclerosis was accompanied by a greenish-brown discoloration of the cornea. Fleischer (Münch. med. Woch., June 1, 1909).

In 378 cases of interstitial keratitis among his 48,000 patients, the cornea sometimes recuperated and became normally transparent again, leaving at most transient astigmatism or myopia. This restoration of transparency is particularly striking after total opacity from ophthalmia neonatorum. J. Santos Fernandez (Cronica Medico-Quir., Havana, Nov., 1917).

**Congenital Pigmentation of the Cornea.**—**Waardenburg** (Nederlandsch Tijdschrift v. Geneesk., Amsterdam, Nov. 30, 1918, 2, No. 22) reports several cases of melanosis of the cornea. He is inclined to regard the pigmentation as merely a displacement of pigment, not an actual melanosis. No instance is known of cancer developing in an eye thus affected. He saw no evidences of a familial or hereditary character of the anomaly, and it did not seem to interfere with vision. The symmetrical pigmentation in one or both eyes was in the form of dark brown stripes, horizontal or vertical, or a stippled area. The iris was gray or brown.

**Treatment of Corneal Opacities.**—Haziness of the cornea due to inflammatory deposit tends to clear up at first rapidly and then more slowly after the subsidence of the inflammation causing it. This tendency to clear up may be accelerated, or continued after it would otherwise cease, by certain applications

to the cornea. One of the most valuable is the daily instillation of a solution of **dionin**, 1 to 5 per cent., or the application of that drug in powder, once in two or three days.

**Iodine vasogen** is a valuable application in infiltrated and spreading ulcers of the cornea, whether associated with purulent conjunctival secretion or not. It is particularly indicated in those cases in which the galvanocautery is contraindicated by the stimulation of the infiltrate. It rarely causes pain, if not applied in excess, and never causes any unpleasant reaction or untoward effects. Preliminary anesthetization of the cornea with cocaine is rarely required, and, in general, is better omitted. The application is best made every other day until the infiltrate begins to shrink decidedly, and then should be made every three or four days until the infiltrate disappears. Alexander Duane (Archives of Ophthalm., vol. xxxi, No. 5, 1902).

The peculiar action of **dionin** on the conjunctival membrane has been quite extensively utilized in ophthalmological practice. The drug produces a marked conjunctival edema. The increased quantity of lymph produced, aids in carrying away the products of inflammation, and explains the therapeutic success of dionin in various eye diseases. The writer reports the results of his experience with dionin in corneal opacities. The beneficial action of the remedy varies according to the dimensions of the opacity and its depth. The application of dionin for three or four days is indicated in all varieties of the disorder. A more persistent use of it rarely leads to success. It may, however, be employed over longer periods in interstitial keratitis, best in the form of a 5 per cent. ointment with **yellow oxide of mercury**, to be used at bedtime. G. Vajda (Orrosi Hetilap, vol. xlv, No. 52, 1902).

Primary opacity of the cornea from the action of lime or other metallic



caustics can be cleared up by chemically dissolving the opaque tissue. The best measure for the purpose is a mixture of **ammonium chloride** and **tartaric acid**. This is applied to the cocainized eye, beginning with a 4 per cent. solution of ammonium chloride, to which from 0.02 to 0.1 per cent. tartaric acid is added. The ammonium chloride can be increased to 10 per cent. and more, but no more tartaric acid should be added. Guillery (*Deut. med. Woch.*, June 25, 1908).

One of the oldest, the dusting of **calomel** upon the surface, is still useful in the opacities left by phlyctenular keratitis. Other irritants have been used in a similar manner. **Massage of the cornea**, either by rubbing through the closed lid or by stroking and rubbing the cornea with a corneal spatula, or specially devised instrument, has also a positive effect in renewing the process of absorption when this becomes sluggish.

By the term "**pressure inunction**" the author designates a form of treatment involving **mercurial inunction** combined with more or less continuous pressure, and found useful by him in chronic hyperplastic conditions of the cornea, sclera, and vitreous body.

The ointment used consists of 30 grains (2 Gm.) of calomel in 1 ounce (32 Gm.) of petrolatum. It should be rubbed up very carefully so that no particles remain undivided. It is applied freely to the closed eyelids; in cases of corneal opacity the conjunctival sac should be filled also. A pad of absorbent cotton is placed over it, and three or four turns of a good elastic flannel bandage then applied rather tightly. This dressing is used from two to three hours daily.

The cases most benefited by this treatment are those of corneal opacities of a dense type, interstitial deposit, plastic deposit on the lens from iritis, opacities of the vitreous, and

some obstinate cases of scleritis. The improvement is slow and the treatment must be persisted in for some months, but results which could not be hoped for under other methods were obtained by the author through its use. Mercurialization never resulted from the treatment. G. Sterling Ryerson (*Canada Lancet*, June, 1912).

**Electrolysis** is also of marked value in clearing up such opacities, if they are unattended with anterior synechiae, and especially if due to infiltration of the cornea rather than repair of extensive loss of substance by ulceration.

When it is impossible to secure further absorption of the opacity, it may be rendered less noticeable and annoying by **tattooing** the affected region. Sometimes tattooing is done to render entirely opaque a part of the cornea which is only hazy, and so admits to the eye diffuse light that impairs vision.

**CORNEA, TUMORS OF.**—New growths situated wholly or chiefly in the cornea are rare. They may be of importance because of the disfigurement they produce, from interference with vision, or by danger of extension when of a malignant character.

Histological description of the enucleated eye of a man aged 20 who had a large, congenital, yellowish-white tumor of the cornea of the size of a hazelnut, over which he could not close the lids. The eye was of normal tension, not irritated and not painful, but blind. The dermoid occupied the whole cornea and encroached upon the sclera. The iris touched, and partly lay in, the lower half of the cornea; also the shrunken, partly calcified lens. R. Tischner (*Klin. Mon. f. Aug.*, July, 1911).

Frequently tumors of the conjunctiva extend over the cornea, and so belong partly to both regions. It has even been doubted whether primary tumors of the

cornea ever occur. But well-attested cases are on record. The most frequent form of corneal tumor is the dermoid, which usually starts about the sclero-corneal junction and extends both ways. It is generally believed to be always congenital; but may slowly increase in size for many years; such tumors are commonly removed for cosmetic reasons.

*Papilloma* commonly starts in the conjunctiva, but it may spread over the whole surface of the cornea. The growth is vascular, and in minute structure resembles a cauliflower. If completely removed and its base touched with nitric acid it shows little tendency to recur.

Malignant neoplasms involving the cornea are usually secondary. Perhaps carcinoma of the cornea is always secondary to such growths of the conjunctiva or some more distant part. Fibroma or sarcoma may be primary.

Corneal scars, although often permanent, and, if large, subject to distention, very rarely become the seat of keloid changes. But a tumor of that kind is possible.

EDWARD JACKSON,  
Denver.

**CORNUTOL.** See ERGOT.

**CORPUS LUTEIN.** See ANIMAL EXTRACTS.

**CORROSIVE SUBLIMATE.**  
See MERCURY.

**CORYZA.** See ACUTE RHINITIS.

**COTARNINE** is an alkaloid obtained by the oxidation of narcotine, one of the alkaloids of opium. It is used in the form of *cotarnine hydrochloride* and *cotarnine phthalate*, the former being official.

*Cotarnine hydrochloride*, the trade name of which is *stypticin*, is the cotarnine salt of hydrochloric acid, produced by the action of oxidizing agents upon narcotine. It is a yellow, crystalline powder, having an

intensely bitter taste, and soluble in water and alcohol.

*Cotarnine phthalate*, the trade name of which is *styptol*, is the cotarnine salt of phthalic acid, obtained from narcotine by oxidation with dilute nitric acid and combined with phthalic acid to form a neutral salt. It is a yellow, microcrystalline powder, very readily soluble in water.

**PREPARATIONS AND DOSE.**—*Cotarnine hydrochloridum*, U. S. P. (cotarnine hydrochloride) may be administered in the dose of  $\frac{3}{4}$  grain (0.05 Gm.) four or five times a day. It is best given in the form of pills, capsules, or coated tablets on account of its bitter taste. For hypodermic injection 32 minims (2 c.c.) of a 10 per cent. solution may be employed. A pure or strong solution may be used locally.

*Cotarnine phthalas* (cotarnine phthalate) is given in the dose of  $\frac{3}{4}$  grain (0.05 Gm.) three to five or even nine times daily if necessary. For subcutaneous injection 3 grains (0.195 Gm.) dissolved in 30 minims (1.85 c.c.) of water may be used. It may also be employed in the form of a dusting powder.

**PHYSIOLOGICAL ACTION.**—Cotarnine hydrochloride is similar in action to hydrastinine. It has hemostatic and analgesic properties and is a uterine sedative. It is said to act first as an excitant and then as a paralyzant to the respiratory center. Falk, of Berlin, claims that it is a paralyzant to the motor side of the spinal cord.

Cotarnine phthalate resembles cotarnine hydrochloride in action, but has more active hemostatic properties. It is also said to have pronounced sedative properties.

**THERAPEUTICS.**—Cotarnine hydrochloride may be used locally, as a styptic. In functional **dysmenorrhea** it is said to be particularly useful. It has been recommended in **hemorrhage due to threatened abortion**, and is said to be of value in all **uterine hemorrhages** not due to fungus, neoplasm, or particles of retained placenta. It may also be employed in **epistaxis**, **hemorrhage after extraction of a tooth**, and **bleeding from the bladder**.

Cotarnine phthalate may be applied locally as a dusting powder. It is said to be useful in all forms of **uterine hemor-**

**rhage.** It is useful in the hemorrhages of uterine cancer.

The special field of cotarnine is in the control of **uterine hemorrhage**, especially that occurring in connection with fibromas. It may also be employed in **dysmenorrhea** and in the irregular menstruation of the **menopause**. It is less useful in post-partum **hemorrhage**, and is believed to act upon vasomotor nerves of the uterus rather than upon the uterine muscle. The writer reports 6 instances of persistent uterine hemorrhage in which the ordinary remedies failed; 5 of these, including 2 of obstinate bleeding after absorption, responded quickly to **cotarnine phthalate**. C. A. von Ramdohr (N. Y. Med. Jour., vol. lxxxv, p. 438, 1907).

As compared with epinephrin, the salts of cotarnine (styptol and stypticin) and cotarnine phthalate are inferior hemostatics. Hanzlik (Jour. of Pharm. and Exper. Therap., Jan., 1918). H.

**COTTONSEED OIL** is a vegetable oil expressed from the seeds of *Gossypium herbaceum* Linné, and then purified. The Egyptian seed contains about 25 per cent. of the oil, while the American seed contains not more than 20 per cent. The oil, as it is expressed, has a dark-brown color and turbid appearance, while the refined oil is a clear, straw-colored fluid having a faint earthy odor, and a pleasant, nut-like taste. It is slightly soluble in alcohol, but readily soluble in ether, chloroform, and carbon disulphide. Cottonseed oil contains palmitin, olein, and coloring matter.

**PREPARATIONS AND DOSE.**—*Oleum gossypii seminis* (cottonseed oil) is given in the dose of 4 fluidrams (16 c.c.). It is also used externally, and is a constituent of the official *linimentum ammonia* and *linimentum camphoræ*.

**PHYSIOLOGICAL ACTION.**—Cottonseed oil is mild, non-irritating, said to be nutrient, laxative, and emollient.

**THERAPEUTICS.**—Cottonseed oil is mostly used to adulterate other and more expensive oils. It may be used for the same purpose that olive oil is employed when the latter proves too expensive for the patient. H.

**COUNTERIRRITATION** is the production of an area of superficial inflammation of a part of the body to produce a good result on a more distant diseased part. It acts reflexly through the nervous system. An impulse is carried from the part to which the agent is applied to the nerve-center, and thence to the trophic nerve, which causes various changes in the diseased part.

Hare gives the following uses of counterirritation: for the effect on congestions and inflammations; to cause the absorption and removal of inflammatory deposits after true inflammation has ceased; for the relief of pain; for the effect on the general system by the use of blisters.

For the production of severe counterirritation escharotics may be used, as caustic soda, lunar caustic, antimonial ointment. Silver nitrate has been employed in **incontinence of urine**, a solution being painted around the meatus urinarius.

Blisters are much less severe and are more often used than the escharotics, the cantharidal blister being usually employed. The blister should not be applied directly to an acutely inflamed area. Blisters are of value in **acute pleurisy** and in **pneumonia**. When applied over the sacrum they have afforded good results in **vesical paralysis**. They may be applied along the vertebral column in **abdominal pain** and **pleurodynia**. Simon, of Dublin, has employed blisters in **chorea**, applying them to the most affected side. Blisters may also be used in **cerebritis**, **peritonitis**, **inflammation of joints**, chronically inflamed **glands**, **bronchitis** in children, and in **erysipelas** (see **CANTHARIDES**). Iodine and iodine ointment may be used for **effusions in joints** and for **enlarged glands** before pus has formed.

Rubefacients may also be resorted to to produce counterirritation—usually for the relief of **pain**. For this purpose mustard, capsicum, spice plaster, and turpentine stupes may be used.

The mustard plaster is made by mixing equal parts of mustard and wheat flours and moistening with water or vinegar. It is of value applied to the nape of the neck in **headache** and **cerebral congestion**.

It may also be used in **inflamed joints and muscular rheumatism**. Capsicum in the form of the plaster or the tincture is employed as a counterirritant in the same conditions in which the mustard plaster is used. The spice plaster is useful in **gastrointestinal conditions of children**; the turpentine stupe is also of value in **deep-seated inflammations**. H.

**COW-POX.** See VARIOLOID AND VACCINATION.

**CRAW-CRAW.**—This term, a phonetic reproduction of the expression "kra-kra," which natives of the West Coast of Africa use for most pruriginous affections of the skin, is a form of nodular dermatitis met in Africa, Ceylon, and other tropical countries. It consists in the presence of a multitude of hard, round, or oval, itching papules, varying in size from that of a millet seed to that of a small pea. It affects principally the extremities, but may extend to the trunk, though respecting, as a rule, the head. Apart from the lesions, due to scratching, the papules do not ulcerate, but tend to exfoliate, leaving irregular areas of hyperpigmentation. The disease resembles scabies; Castellani and Chalmers, in fact, state that most of the cases of so-called "craw-craw" are instances of neglected scabies or *tinca corporis*. Still, O'Neil states that it subsides in a cooler climate, to recur when the subject returns to the tropics.

**ETIOLOGY AND PATHOLOGY.**—O'Neil found minute, filaria-like organisms in the papules. Nielly found nematode embryos in the blood of a French boy—a discovery which led Manson to feel justified in the belief that the cutaneous parasite was an advance developmental form of the embryo in the blood. Manson also suggested that the microfilaria observed by O'Neil might have been *Filaria perstans*. On the whole, the pathogenic factor of the disease is still obscure.

**TREATMENT.**—The regular application of a **salicylic spirit lotion** (2 per cent.) followed by **B-naphthol ointment** (5 to 10 per cent.) during a long period causes marked improvement and sometimes a cure, according to Castellani and Chalmers. **Ichthyol** and **belladonna oint-**

**ment** is also useful in some cases. Internal medication does not seem to prove helpful. S.

**CREOLIN.** See CRESOL.

**CREOSOTE (CREASOTE).**—Commercial creosote is obtained by the dry, fractional distillation of wood tar, or from crude pyroligneous acid. Medicinal creosote is, or should be, obtained by the distillation of the tar of the beech (*Fagus silvatica* or *fer-ruginca*). The substance is a complex mixture of compounds allied to phenol, and including chiefly guaia-col [ $C_6H_4(OCH_3).OH$ ] and creosol [ $C_6H_3.CH_3.(OCH_3).OH$ ], together with minute amounts of phlorol [ $C_6H_4.C_2H_5.OH$ ], xylanol [ $C_6H_3-(CH_3)_2.OH$ ], cresol [ $C_6H_4(CH_3).OH$ ], phenol [ $C_6H_5OH$ ], etc. The last two substances named, which have a lower boiling point than the others, are largely eliminated in the process of preparation,—a circumstance to which creosote owes in great measure its own special therapeutic utility.

Pure creosote is a nearly colorless, oily liquid possessed of a burning taste and a disagreeable penetrating, smoky odor which is most characteristic. Its specific gravity is officially required not to be less than 1.078 at 25° C., but many samples fall below this limit. Although another requirement is that it should not become brown on exposure to light, Gane asserts that all commercial creosotes darken under these conditions. With age the substance acquires a yellowish hue, and upon prolonged exposure to light and air it becomes of a deep reddish-brown color, when it is unfit for medicinal use.

Creosote is but slightly miscible with water. In 120 parts of hot water it forms a clear liquid, but, upon cooling, a turbidity appears, which is due to the separation of small droplets of the oil. In 140 to 150 parts of cold water it forms a turbid mixture. It is soluble in all ratios in absolute alcohol, ether, chloroform, glacial acetic acid, and fixed and volatile oils. In reaction to litmus, creosote is neutral or very slightly acid. When ignited, it burns with a smoky flame.

Crude phenol is not infrequently substituted for beechwood creosote, to which it bears some chemical relation ("coal-tar creosote"). The fraud may be readily detected from the fact that the crude phenol is soluble in glycerin, while creosote is not. Again, creosote, mixed with an equal volume of collodion in a dry test-tube, does not give a gelatinous precipitate of nitrocellulose, while crude phenol does. Finally, upon adding a drop of a 10 per cent. solution of ferric chloride to 10 c.c. (2½ drams) of a saturated aqueous solution of creosote, transient violet-blue and grayish-green colorations will appear, while if "coal-tar creosote" be present instead the ultimate muddy-brown color will develop at once.

#### PREPARATIONS AND DOSES.

—The only official preparations are:

*Creosotum*, U. S. P. (creosote). Dose, 1 to 20 minims (0.06 to 1.25 c.c.); average, 3 minims (0.2 c.c.).

*Aqua creosoti*, U. S. P. (creosote water), made by agitating vigorously 1 part of creosote with 99 parts of water, but containing somewhat less than this ratio of creosote in true admixture. Should be freshly prepared when dispensed. Dose, 2 fluidrams (8 c.c.).

The following ointment is recognized in the National Formulary:—

*Mulla creosoti salicylata*, N. F., creosote, 10, and salicylic acid, 20 per cent.

Official in the British Pharmacopœia are:—

*Mistura creosoti*, B. P. (creosote mixture), a 0.2 per cent. watery solution flavored with spirit of juniper and sweetened with sugar. Dose, ½ to 1 fluidounce (15 to 30 c.c.).

*Unguentum creosoti*, B. P. (creosote ointment), a 10 per cent. preparation.

The following derivative is now officially recognized:—

*Creosoti carbonas*, U. S. P. (creosote carbonate; creosotal), a mixture of carbonic acid esters prepared from creosote by treating the latter in solution in sodium hydroxide with carbonyl chloride, and containing 92 per cent. of creosote. It occurs as a yellowish, clear, viscous liquid, odorless and with a slightly bitter, oily taste. It is not soluble in water, but dissolves in alcohol, ether, and fixed oils. It is stated to have the same action as creosote, but to be devoid of caustic and toxic power. Dose, 15 grains (1 Gm.).

*Creosote benzoate*, a yellowish liquid, soluble in alcohol and ether. Used locally only, as an antiseptic in rhinology.

*Creosote oleate* (oleocreosote), a yellowish, oily liquid, soluble in ether and chloroform. Dose, 15 to 45 minims (1 to 3 Gm.).

*Creosote phosphite* (phosphotal), a reddish-yellow, oily liquid, with a faint odor of creosote and a pungent taste. Contains about 90 per cent. of creosote, and dissolves readily in water and alcohol. Dose, 3 to 15 minims (0.2 to 1 c.c.).

*Creosote tannate* (tannosal; tanosal;

creosal), a dark-brown, very hygroscopic powder, with the odor and taste of creosote, of which it contains 60 per cent. It is soluble in water, alcohol, glycerin, and acetone, and insoluble in ether. Dose, 5 to 30 grains (0.3 to 2 Gm.).

*Creosote valerate* (creosote valerianate; eosote), a yellowish, oily liquid, of smoky-aromatic taste and odor, insoluble in water, readily soluble in alcohol and ether. Dose, 3 to 10 minims (0.2 to 0.6 c.c.).

*Calcium creosote*, prepared from equal parts of creosote and calcium hydroxide by percolation, enough water being used to form a 5 per cent. solution, of specific gravity 1010 to 1012. There results a reddish-yellow fluid, which becomes brown on keeping, has the odor of creosote, a sharp taste, and a strongly alkaline reaction, but is not irritating (Kolipinski). Dose, 2 fluidrams (8 c.c.).

*Creosol* (homoguaiacol), a colorless to yellowish, aromatic fluid, slightly soluble in water. Used externally as antiseptic and astringent.

**MODES OF ADMINISTRATION.**—Creosote is best administered in capsules, which do away with its disagreeable odor and prevent any injurious effects on the mucous membranes of the mouth and pharynx. It may also be given in some fluid preparation, e.g., in an emulsion, in an elixir, or in codliver oil (creosote, 15; rum or codliver oil, 1000 parts). Whitla found the following palatable creosote mixture:—

℞ *Creosoti*,  
*Acidi acetici glacialis*,  
 āā ..... ℥xv (1 c.c.).  
*Spiritus juniperi* ..... ℥xxx (2 c.c.).  
*Syrupi* ..... f℥j (30 c.c.).  
*Aque destillata* ..... f℥xv (450 c.c.).

M. Sig.: One to two ounces at a dose.

In any fluid preparation a dilution of 1:200 is advisable.

Creosote is best given as follows: For each drop of the creosote there should be a tablespoonful of hot water. The creosote should then be thoroughly emulsified by actively stirring with a spoon for at least five minutes. As the larger doses are reached (15 to 20 drops—0.9 to 1.25 c.c.) the amount of water need not exceed a tumblerful; with the larger doses a rapid and thorough emulsification can be obtained by the use of a lemonade shaker. The creosote is given fifteen to twenty minutes before meals. When prepared in this way, as much as 20 drops (1.25 c.c.) can be given, three times daily, for weeks or months. H. R. M. Landis (*Progressive Medicine*, vol. ix, No. 4, p. 281, 1907).

Creosote pills had best be avoided. For administration of the drug in cachets, Kopp advises the following:

℞ *Creosoti* (*beechwood*),  
*Benzoini* ..... āā gr. xv (1 Gm.).  
*Carbonis ligni* ..... ℥iiss (6 Gm.).

(The benzoin is to be first powdered, triturated for a few minutes with the creosote, and the charcoal gradually added. The mass is then to be divided into five or ten cachets.)

An excellent way to avoid gastric irritation in administering creosote is to mix the creosote with powdered charcoal in the proportion of 1 part of the former to 2 of the latter by weight. When dry, the powder is put up in wafers, each containing the proper dose of creosote. It might be preferable, merely for convenience, to put the power into capsules. Several of them can be taken at a time if the dose is too bulky to be contained in a capsule small enough to be swallowed readily. It is still better to incorporate the creosote with a generous amount of some bland substance, such as curd soap with powdered licorice or althea, and put the mixture at once into capsules. Bouchet (*Progrès méd.*, Sept. 1, 1906).

Whenever creosote is ordered for internal use, the beechwood variety should be specified.

Creosote may also be administered by inhalation; a mixture of it and phenol with spirits of chloroform, in equal parts, is as good as any (Dixon).

The drug has been given subcutaneously or intramuscularly, but with these modes of introduction considerable local pain is likely to follow, and the therapeutic results, on the whole, have not encouraged further attempts in this direction in preference to oral administration.

Hypodermic injections of creosote given twice a week in six cases of **pulmonary tuberculosis**. The patients, if only transiently, showed improvement in the hacking cough, sleep, and general condition. The injections were, however, painful. At the fifth or sixth injection the whole series of patients developed superficial and benign abscesses, readily healing, but terminating the treatment. I. Van Gieson and H. L. Lynch (Med. Record, May 11, 1912).

Creosote carbonate, though acting somewhat more slowly than creosote, may be substituted for it, probably with advantage, since it is generally believed to be better borne by the stomach than the uncombined substance. It may be given in capsules, or in milk, coffee, chocolate, wine, brandy, whisky, simple elixir, codliver oil, or in an emulsion.

The advisability, in prescribing uncombined creosote, of employing only *small initial doses*, of the drug was well shown in a case reported by Zawadzski, in which a woman 42 years old was ordered creosote in doses, from the start, of 6 drops three times daily in milk. After she had taken three doses typical symptoms of severe poisoning appeared, and

death took place four days later. Though in this case a marked idiosyncrasy to the drug probably existed, the author seems justified in his advice not to order more than 1 or 2 drops at the beginning, but increase the dose gradually later. He expresses the opinion that creosote should not be given in milk, in which it is insoluble, acting as if undiluted.

*In children*, Hock found, upon attempting to administer creosote with tincture of gentian, that the stomach almost always rebelled after a few days. He was most successful with a 1 or 2 per cent. solution of the drug in codliver oil, to which 0.05 per cent. of sugar was added. The dose of the mixture given was from  $\frac{1}{2}$  fluidram (2 c.c.) to  $\frac{1}{2}$  fluidounce (15 c.c.) three times daily. Creosote carbonate affords a very advantageous method of administration in children.

**INCOMPATIBILITIES.** — Creosote is incompatible with albumin, acacia, strong nitric or sulphuric acid, and salts of silver, iron, and copper. An explosion results if creosote be mixed with silver oxide.

Creosote carbonate is incompatible with alkalies, which set free the creosote.

**CONTRAINDICATIONS.** — The administration of creosote should not be continued in cases where it is the obvious cause of gastric disturbances, of albuminuria, or of smoky urine. It is also contraindicated in all febrile cases of lung tuberculosis in which the temperature is 100° F. or more, in progressive cases, and in patients with blood-tinged sputum or those known to be subject to hemoptysis (Fishberg).

**PHYSIOLOGICAL ACTION.** — *Locally*, creosote acts much as does

phenol, being analgesic, antipruritic, astringent, caustic, and strongly antiseptic and germicidal. Many observers believe it more powerful than phenol in the last-named respect. It is somewhat less of an irritant, however, than phenol, and as an antiseptic it is among the most energetic agents known (Wood).

*Internally* administered, creosote acts in small doses as an expectorant and sedative to the stomach. It has also been said to increase the coagulability of the blood. When continuously used, it tends to improve the appetite and nutrition in general. In large doses, creosote acts as a depressant to the nervous and circulatory systems; like phenol, strongly irritates the mucous membranes, and may, if so administered as to be rapidly absorbed, *e.g.*, subcutaneously, produce a fall in the body temperature.

Even when taken by mouth, creosote is rather promptly absorbed. It soon combines in the system with sulphuric acid to form non-toxic conjugate sulphates—guaiacol sulphate and creosol sulphate of potassium—and is eliminated in this form, chiefly in the urine, probably to a slight extent also by the mucous membrane of the bronchi. According to the researches of Imbert, the greater part of a dose of creosote is thrown out during the first twelve hours after its administration. The guaiacol element appears to be the most rapidly eliminated.

Creosote carbonate acts in the same manner as creosote, but is somewhat less rapidly absorbed. According to Reiner, this compound has, in many cases, a tendency to diminish secretion; it seems to have no influ-

ence upon peristalsis. Occasionally it causes fluid stools, but this effect vanishes in a day or two; in a few other cases, it appears to induce intestinal sluggishness. Eructations and vomiting appear only after large doses, and even then rapidly disappear without withdrawal of the remedy. Like creosote, the carbonate tends to increase the appetite, diminish and deodorize the secretions of the bronchi and kidneys, and exert a favorable effect upon nutrition.

#### CREOSOTE POISONING.—

When toxic amounts of creosote are ingested the symptoms resemble those produced by phenol. There is persistent burning in the throat and stomach, vertigo, later unconsciousness, with marked cardiac enfeeblement, vasomotor and respiratory depression, and lowered body temperature. The urine is likely to be "smoky" or black in color. The reflexes are abolished, the skin is cold and clammy, and the odor of the drug may be noticed. Death may occur from respiratory failure, and the heart ceases its function in diastole.

Case of a woman 35 years of age who took by mistake 25 Gm. (6¼ drams) of creosote carbonate and soon after became unconscious. An hour and a half after the ingestion of the drug, the **stomach was washed out** until the evacuated liquid lost the characteristic odor. Some hours later there was further evacuated, through vomiting and lavage, a blood-stained fluid having the odor of creosote. This showed that a portion of the creosote carbonate absorbed was eliminated as creosote through the gastric mucous membrane and had exerted a caustic action on it. The urine in this case was greenish black, showed no albumin, and contained large amounts of conjugate sulphates. The patient recovered in spite of the



gravity of the poisoning. Stadelmann and Boruttau (Munch. med. Woch., Nu. 39, 1907).

The possible untoward effects of *therapeutic* doses of creosote are manifested chiefly in gastrointestinal disturbances and in discoloration of the urine. Browning has reported 2 cases in which temporary deafness was produced by full doses of the drug. Some individuals appear to be much more susceptible to its action than others. Thus, in 2 patients of Nimier in whom 30 minims (2 c.c.) of creosote were given daily by rectum, the urine would become black after standing a short time. In a case reported by Graham, on the other hand, the dose, 1 minim (0.06 c.c.) by mouth, thrice daily at first, was rapidly increased until 340 minims (21 c.c.) were being ingested daily, and 3 to 4 fluidrams (12 to 14 c.c.) were then taken for two and a half months without any ill effects. It would seem not unlikely that in some instances untoward effects attributed to creosote have arisen merely because of substitution for the beechwood variety of the more irritating and toxic "coal-tar creosote" or crude phenol.

Fishberg points out the fact that creosote, upon continuous use, is capable of giving rise to symptoms resembling those produced by the injection of tuberculin in tuberculous patients, especially feverishness, malaise, and evidences of renewed morbid activity at the seat of disease. He considers creosote contraindicated, therefore, in all febrile cases of tuberculosis in which the temperature reaches or exceeds 100° F. (37.8° C.), as well as in all progressive cases, because it is in these that the drug is

most apt to cause general and local reactions.

Creosote often provokes general and local reactions which are analogous to those provoked by tuberculin. Usually with excessive doses, but occasionally also with minimal doses, after taking creosote for several days, the patient is taken with a feeling of chilliness and fever; pain in the limbs, back, and joints; weakness, fatigue, and insomnia. Malaise, gastric disturbances, and even vomiting, in patients whose stomach has before not given any trouble, make their appearance. Quite a considerable part of the creosote ingested is eliminated through the bronchial mucous membrane, and this often excites a focal reaction, which at times reminds one of the focal reaction of tuberculin. In such cases sanguineous expectoration and even hemorrhage are not uncommon, while the lesion in the lungs may be aggravated or even spread. Râles, previously absent or scanty, make their appearance.

If the administration of creosote is persisted in after these symptoms, the condition of the patient may be so aggravated as to render the prognosis hopeless in a case with previously a fair outlook. Smoky urine, like that of phenol poisoning, is now seen; the patient complains of a taste of creosote in his mouth. This may be followed by vertigo, profuse perspiration, chilly sensations, and even cyanosis and collapse, as the author saw in one case, which was greatly relieved by the discontinuance of the drug. Maurice Fishberg (Amer. Pract., Sept., 1912).

**TREATMENT OF CREOSOTE POISONING.**—In the mild cases, arising from therapeutic doses, mere cessation of administration of the drug will suffice. In severe cases, due to frankly poisonous doses, the treatment should be the same as is generally employed in phenol poison-

ing. If the case is seen in time, the **stomach** should be at once **washed out**. **Magnesium** or other soluble **sulphate** should be given as chemical antidote, **atropine** and **strychnine** hypodermically, together with **coffee** by **rectum** and **digitalis**, administered as stimulants, and **morphine** or **opium** given, if required, for the relief of pain. **Heat** should be applied to the body and extremities, and **demulcent drinks** administered.

**THERAPEUTIC USES.** — **Diseases of Respiratory Tract.**—It is in the treatment of affections of the respiratory apparatus that creosote has gained greatest repute. Its elimination by the bronchial mucous membrane, formerly believed to take place to a considerable extent, has recently been questioned by various observers, especially by Bufalini, who from experimental work has formed the opinion that such elimination does not occur. Nevertheless clinical observations of the drug's action have shown it to be a stimulating expectorant of considerable value. This is especially true where there is fetor of the bronchial secretions. Creosote usually distinctly diminishes expectoration and removes its purulency.

Although many observers maintain that the drug exerts a curative effect upon tuberculous lesions, the opinion is frequently expressed that creosote is without definite influence upon the progress of **pulmonary tuberculosis**. It is freely admitted, however, to lessen cough, expectoration, and the tendency to night-sweats, and there is little doubt that it is one of the best medicinal agents available for the treatment of phthisis as well as of certain forms of **bronchitis**, **bronchopneumonia**, and all

conditions associated with **bronchiectasis** or **bronchorrhea**. The opinion is now prevalent that in tuberculosis creosote restrains more particularly the morbid processes due to mixed infection, rather than those arising through the primary infection itself.

The greatest drawback in the use of the drug is the inability of many patients to take it in doses sufficient to be of benefit. Conway, who administered creosote in nearly 400 cases of **tuberculosis**, variously situated, found it most convenient to prescribe the drug in capsules of 2 to 4 minims (0.12 to 0.25 c.c.) mixed with cod-liver oil and always given immediately after meals. After several days complete tolerance was established, and the dose could be gradually increased, according to the following plan: Begin with 2-minim (0.12 c.c.) doses three times daily; in acute cases increase the dose by 2 minims every fourth day until 12 minims (0.75 c.c.) are given at a dose; if the improvement, after several weeks, is not satisfactory, carefully add 2 minims more every eight or nine days until a 20-minim (1.25 c.c.) dose has been reached; then persist with this quantity until the symptoms warrant a diminution in the amount. The largest dose was often given four or five months at a time with the most satisfactory results. The chronic cases, according to Conway, do not generally require so large a dose or so rapid an increase.

Creosote, to be of any benefit in **tuberculosis**, must be used in large doses and must be given for a long time. It is best to start with 1 to 3 minims (0.06 to 0.18 c.c.) and increase the dose 1 minim daily until at least 15 to 20 minims (0.9 to 1.25 c.c.) are taken three times daily. The author

administers the drug in capsules, in wine, or in an emulsion of codliver oil. The treatment should be interrupted from time to time, the creosote being given for four or five weeks and then omitted for a week or ten days. Philip (*Folia Therap.*, Oct., 1907).

Since in not a few instances the simultaneous ingestion of codliver oil will not be desired, some other mode of administration will have to be employed. The following preparation has been recommended:—

**R** *Creosoti* .....  $\text{mij-x}$  (0.12-0.6 c.c.).

*Tinctura gentiana*

*composita* .....  $\text{mxxv}$  (1 c.c.).

*Alcoholis* .....  $\text{mxx}$  (1.25 c.c.).

*Aqua* ....q. s. ad  $\text{f3j}$  (30 c.c.).

Sig.: For one or two doses.

In cases where creosote is tolerated with difficulty or not at all, the substitution of creosote carbonate is indicated. According to Reiner, very large doses, even 300 minims (19 c.c.), can be given without upsetting the digestion. Just at first there may be some nausea or even vomiting, but these soon pass off and do not require abandonment of the drug.

Observations on the action of creosote carbonate in 100 cases of non-tuberculous respiratory disease in infants and children. Most of the cases were of **capillary bronchitis**, **bronchopneumonia** following whooping-cough or influenza, and of affections of the upper air passages. The majority of the patients had already been otherwise treated and were given creosote carbonate when in the subacute stage. It was concluded that the drug possesses a distinct curative action in bronchial and pulmonary affections, whether caused by Fränkel's pneumococcus, Friedländer's pneumobacillus, the streptococcus, the staphylococcus, or other causes. Whether this is due to its preventive influence upon bacterial growth, to a reparative action upon the local process, or to its antagonizing the products of

the growth of the bacteria, it is not possible to say. At all events, in the 100 cases, there were but two deaths, one in a child 8 months old suffering from bronchopneumonia, and the other in a little girl of 3 years with capillary bronchitis, in whom the creosote carbonate had only been given two days. The dosage employed was, in children 1 year old, 1.5 Gm. (24 minims) of creosote carbonate *pro die*; 1 to 2 years, 2 Gm. (32 minims); 2 to 4 years, 2.5 Gm. (40 minims); 4 to 6 years, 3 Gm. (48 minims), and 6 to 10 years, 3.5 Gm. (56 minims). Even in nurslings the drug caused no gastric or intestinal irritation; 3 Gm. (48 minims) were mixed with 80 Gm. (2½ ounces) of raspberry syrup, and given in the course of forty-eight hours. The drug is odorless and is eliminated through the skin and kidneys; the urine becomes dark green or greenish black in color, but does not show the least trace of albumin. K. M. John (*Therap. Monatsh.*, vol. xxi, p. 516, 1907).

Chronic, sluggish, afebrile cases of **tuberculosis**, especially those characterized by profuse expectoration, are often greatly benefited by creosote, intelligently administered. There is often a striking improvement in the digestive functions. An increase in weight is not slow in appearing, which has an excellent effect on the psychic state of the patient.

Another sign of tolerance of creosote is a diminution in the amount of expectoration. Purulent sputum is replaced by odorless mucous material. The cough is greatly ameliorated, and the non-tuberculous **bronchitis**, **tracheitis**, and **laryngitis** frequently met with among consumptives are cured.

In **fibroid phthisis**, characterized by profuse expectoration of pus, creosote is often the best remedy. Cavities often dry up, at least temporarily. Large doses are not at all necessary; 3 to 5 drops (0.18 to 0.3 c.c.) three times a day, given over a prolonged period, produce good and frequently

lasting results. A good product must, of course, be obtained. The author has lately used creosote carbonate almost exclusively and is under the impression that it is more easily tolerated than creosote. It can be given in doses of from 15 to 25 drops (0.9 to 1.5 c.c.) per day. Maurice Fishberg (Amer. Pract., Sept., 1912).

To pyretic cases and those with a tendency to hemoptysis, creosote should rarely be given. Neither should its use be persisted in where constant indigestion is caused, as these patients must, above all else, be kept free from disturbances in the alimentary functions. Subcutaneous administration of creosote, to avoid the evil effects of oral medication, is inadvisable, owing to the pain produced. The rectal route may be tried, although, according to Chaumier, after a few days of treatment in this manner control of the bowel is lost and the patient is frequently attacked by colic and diarrhea. Dor witnessed rapid improvement in cases of **tuberculosis** in the first and second stages to whom intratracheal injections of 1:20 creosoted oil were given; these injections were admirably borne by most of the patients, and 30 minims (2 c.c.) of the drug were administered twice daily. Experiments showed that the oil actually reached the alveoli, and remained there two weeks. The injections, according to the author, should be practised during many months, the patients being auscultated at frequent intervals for the bubbling râles, indicating proper penetration of the drug, and, if necessary, placed in positions facilitating such penetration. Inhalations of creosote, along with other remedies, are strongly recommended

by Lees and Beverley Robinson. Laumonier and Otis suggest the following formula for this purpose:—

R *Eucalyptolis*,  
*Creosoti*,  
*Olei terebinthinae rectificati* .....āā f3v (20 c.c.).  
*Ætheris* ..... f3i¼ (5 c.c.).  
 M. Sig.: To be inhaled.

By the combined, persistent use of beechwood creosote internally and by inhalation, no matter what the stage of the disease, much relief to symptoms may be obtained in nearly all cases. Creosote is of great value as a preventive when **pulmonary tuberculosis** is a menace to the individual, either by reason of constitutional tendency, exposure to infection, or both. To judicious rest, when required, fresh air, and proper food, add creosote, with or without lime salts, and there is at present little or nothing further to insist on. B. Robinson (Med. Record, Nov. 20, 1909).

Following formula recommended for continuous antiseptic inhalation in **pulmonary tuberculosis**:—

R *Creosoti*,  
*Phenolis* .....āā 3ij (8 c.c.).  
*Tinctura iodi*,  
*Spiritus ætheris* .āā 3j (4 c.c.).  
*Spiritus chloroformi* ..... 3ij (8 c.c.).—M.

Two Yeo inhalers are procured, so that they may be used on alternate days and properly cleansed by immersion in boiling water and careful drying. The patient is instructed to pour 6 to 8 drops (0.36 to 0.48 c.c.) of the solution on the felt of the inhaler *every hour* during the daytime, and once or twice during the night if he happens to wake. Nearly all patients soon become accustomed to wearing the inhaler at night. The object should be to keep the piece of felt constantly saturated with the solution, but so that none of it wets the framework of the inhaler itself. The base of the inhaler should be carefully wiped before it is applied,

and a little vaselin or lanolin cold cream smeared over the nostrils and upper lip at first. Of 70 cases treated with inhalations, in conjunction with appropriate dietetic measures, correction of gastrointestinal disturbances, and careful disinfection of the mouth four times daily, 48 recovered completely, 3 were probably complete recoveries, and 10 were incompletely cured. D. B. Lees (Lancet, Nov. 9, 1912).

W. S. Gordon advises the following combination for the relief of **bronchial irritation in tuberculosis**:—

℞ *Creosoti* (beech-wood) ..... ℥j (0.06 c.c.).  
*Olei santali* ..... ℥v (0.3 c.c.).  
*Terpini hydratis* ... gr. ij (0.12 Gm.).

Ft. in capsulam no. j.

Sig.: One capsule three or four times daily.

In **chronic bronchitis** creosote is not infrequently a useful remedy. The inhalation of steam impregnated with creosote, 10 to 20 minims (0.6 to 1.2 c.c.) to a pint (500 c.c.) of hot water (140° F. or 60° C.), tends to lessen overabundant expectoration and will also generally remove fetor of the breath, where it is present. In children doses of 1 to 3 minims (0.06 to 0.2 c.c.) of creosote (beechwood only) or creosote carbonate in larger amounts will often produce good effects where other remedies have failed. In adults the dosage should be gradually increased to 5 minims (0.3 c.c.) three or even more times daily.

Similarly, in **pulmonary abscess** or **gangrene**, the continuous inhalation of a mixture in equal parts of creosote, alcohol, and spirit of chloroform is of considerable value as an antiseptic and deodorizing measure. Increasing doses of the drug should simultaneously be taken *per os*.

In **pneumonia**, the expectorant qualities of creosote are sometimes availed of. Casati, who gave the drug to 26 cases, beginning on the third day, witnessed recovery in all, and states that the patients receiving creosote appeared to recover more rapidly and thoroughly than those treated in other ways.

Nine cases of **pneumonia** both of the lobar and lobular variety in which creosote carbonate was employed. The oldest patient died from myocarditis, all the others recovering. The drug was administered in capsules containing 10 minims (0.6 c.c.) six times a day, in some cases for as much as eight days. There were no symptoms of depression or gastrointestinal disturbance. In all the cases the temperature fell as soon as the patient was under the influence of the drug, and there was the same improvement in general condition which usually supervenes on the crisis. It is doubtful, however, whether the course of the disease was actually shortened. Leonard Weber (Med. Record, Nov. 2, 1901).

A large percentage of cases of **pneumonia** are cut short or aborted, almost all are mitigated, and only very few are not benefited by creosote. It is important that the drug should not be discontinued as soon as the active symptoms subside, as there may be a recurrence. The carbonate is the best form. Guaiacol and its salts do not seem to exert the same action. J. L. Van Zandt (Southern Pract., Dec., 1901).

Circulars sent to medical journals and individuals with request for information concerning the effect of creosote in **pneumonia**. Replies were received from 75 sources, representing 1130 cases. Of these, 56 ended fatally—a mortality of less than 5 per cent. About half of those replying were of the opinion that creosote can abort pneumonia; the reporters were almost unanimous in claiming that the disease was mitigated by the use of

the drug. J. L. Van Zandt (Med. Record, Oct. 18, 1902).

Creosote carbonate used in 67 cases of **pneumonia**. In no case was there vomiting or any disturbance of the digestion; no disturbance of the urine was noted. The degree of toxemia in all cases, barring the fatal ones, was mild. In the cases treated pseudocrises were common, but bore no relation to the crisis or the mortality. The mortality percentage (14.9) secured did not corroborate the unusually low figures obtained by Wilcox, Van Zandt, and others. Scott and Montgomery (Therap. Gaz., Dec. 15, 1903).

Calcium creosote used with good results in various infections. In **croupous** or in **broncho-pneumonia** it should be given at two-hour intervals without interruption. For an adult the dose is 2 to 4 drams (8 to 16 c.c.) in a tumblerful or less of water; for a child of 6 to 8 years, 1 dram (4 c.c.), and for an infant of 1 year, from 3 to 5 drops. These quantities can often be given day and night. An adult is thus able to take about 4 fluidounces (120 c.c.) *pro die*,—a quantity equivalent to 96 drops (6 c.c.) of creosote. In **pneumonia** the remedy tends to cut short the disease, reduce the fever, slow the respiration and pulse, and facilitate and increase the cough. Other affections in which the compound was found useful were **typhoid fever**, **cholelithiasis**, **tuberculous diseases of the bones and joints** in children and adolescents, **Pott's disease**, **tuberculous lymphadenitis**, **scrofulous keratitis**, the **summer diarrhea of infants**, and **hemorrhoids**. L. Kolipinski (Monthly Cyclo. and Med. Bull., June, 1909).

In **whooping-cough** considerable relief is often afforded by inhalations of creosote, especially when the cough is violent and protracted, and the secretions scanty or hard to bring up. The remedy is best employed with a croup-kettle; it is placed on a sponge

in the neck of the spout and brought to the patient under a tent formed by throwing a sheet over the crib or over chairs suitably placed (Hamill). The patient's eyes should be protected with a bandage. Internally, Hock has had good results with creosote in treating the sequelæ of whooping-cough, and also in the catarrh which frequently follows **measles**.

**Gastrointestinal Disorders.**—**Anorexia** is sometimes relieved by the internal use of creosote in small doses, a property chiefly utilized in **pulmonary tuberculosis**, in which the drug is usually combined with the compound tincture of gentian. **Vomiting** is another symptom which creosote may overcome, especially where it is due to unusual irritability of the mucous membranes, as in the **vomiting of pregnancy**. In **gastric pain** the drug exerts the same analgesic effect as would phenol.

Beechwood creosote, in from 3- to 10- or 15- minim doses (0.18, 0.6, or 0.9 c.c.), largely diluted and well shaken or stirred, *e.g.*, with from 4 to 6 ounces (120 to 180 c.c.) of clear, pure water, and given half an hour or more before meals, acts as an appetizer, aiding digestion by cleansing the stomach and exciting gastric secretion. The author uses it also for intestinal antiseptics, combining it especially with glycerin—teaspoonful doses of the latter—and freely diluting it with water. C. H. Hughes (Med. Council, Nov., 1908).

Its chief value, however, in affections of the alimentary tract is as an antiseptic. In **fermentative dyspepsia** doses of a few minims, given after meals, tend rapidly to destroy the causative organisms, and with them the gas production and subjective discomfort. In the **diarrheas** of children and infants, especially those preva-

lent in the heated term, and in **cholera morbus**, the drug is of considerable utility as an intestinal antiseptic. Creosote carbonate is, perhaps, to be preferred to creosote in this connection, since, in view of its slow decomposition and absorption, a greater proportion of its effect is exerted in the intestinal tract. Creosote has also been employed in **tropical diarrhea** and **dysentery**. Zangger has recommended the following mixture in the treatment of **infantile gastroenteritis** and various **dyspeptic conditions** in adults:—

<b>R</b> <i>Creosoti</i> ( <i>beech-wood</i> ) .....	℥iij (0.2 c.c.).
<i>Alcoholis</i> .....	℥xv (1 c.c.).
<i>Acacia pulveris</i> ....	℥iiss (10 Gm.).
<i>Syrupi</i> .....	℥j (30 c.c.).
<i>Aqua aurantii</i> .....	℥iiss (10 c.c.).
<i>Aqua</i> .....	q. s. ad ℥iiss (100 c.c.).

M. Sig.: One teaspoonful for children, or one tablespoonful for adults, immediately before each meal.

Excellent results obtained by the use of creosote as a preventive of **dysentery**, and in the treatment of **phthisis**, **pneumonia**, and **malaria**. The drug was administered by inunction; 30 minims (2 c.c.) of creosote were mixed with petrolatum or olive oil, and half of this was rubbed vigorously into the axillæ and groins in the morning and half in the evening. Wood (*Indian Med. Gaz.*, April, 1907).

**Genitourinary Diseases.**—In **gonorrheal urethritis**, especially the **chronic** form, creosote may sometimes be substituted with advantage for the more popular **copaiba**, **sandalwood oil**, and **cubeb**. It may be employed both by the mouth and by **intra-urethral injection**.

Larska treated 50 cases of **acute gonorrheal urethritis** with injections of a 2 to 10 per 1000 emulsion of creosote. The discharge quickly dimin-

ished, became mucoid, and then ceased altogether. According to the author, these patients recovered more rapidly than under ordinary methods, and without a single complication or relapse. An anesthetic action on the urethral mucous membrane was noted.

In conditions attended with decomposition of urine in the bladder, including **chronic cystitis**, creosote may be used. Phenyl salicylate and hexamethylenamine are, however, usually more effectual agents.

**Diabetes.**—Beneficial effects have been observed to occur in this disease under the influence of creosote, administered in ascending doses. Valentini reported 2 cases in which 4 drops (0.25 c.c.) daily, gradually increased to 10 drops (0.6 c.c.), caused a complete disappearance of the glycosuria, which a subsequent return to starchy food failed to reawaken.

**Local Uses.**—In a number of skin diseases, such as **psoriasis**, **acne**, **impetigo**, **leprosy**, **tinea circinata**, and **scabies**, creosote may be applied locally as an analgesic and parasiticide, generally in ointments of from 1:10 to 2:1 strength. It presents no advantage, however, over phenol, which is now almost invariably employed instead.

In **erysipelas**, the use of creosote has been especially advised. It may be applied in a 20 per cent. ointment, but is probably more effective if used pure or sufficiently strong to render the cuticle white as soon as it is touched. It should be penciled over the whole of the inflamed surface, and even beyond it. In **phlegmonous** cases the applications should be frequent, and compresses soaked in dilute alcohol, in which a little creosote

sote may be dissolved, kept constantly applied. In **burns**, especially those in which there is free suppuration or excessive granulation during healing, and in **chilblains**, the use of creosote has also found favor.

In **toothache**, the introduction of a little creosote on a bit of cotton in the cavity of the offending tooth will effectually relieve the discomfort.

**Local hemorrhage**, *c.g.*, the superficial bleeding from **wounds**, **leech-bites**, hemorrhage following the extraction of teeth, and especially that taking place in **menorrhagia**, can frequently be arrested with this drug. The creosote water is generally employed for this purpose.

In the treatment of non-specific sloughing and phagedenic **ulcerations**, as well as of mild, indolent ones, creosote meets the same indications as phenol itself. It may be used in strengths ranging, according to the nature of the case and sensitiveness of the part, from 0.2 per cent. up to the pure drug itself. Thus, there may be treated with it conditions such as **fetid otorrhea** or **leucorrhœa**, **puerperal metritis**, discharging **fistulæ**, etc.

**Ulcers of the larynx**, whether tuberculous or not, may be treated by the application of creosote. In **subacute laryngitis** a spray of creosote, 0.2 to 0.4 per cent. in liquid petrolatum, may be used with advantage. In **laryngeal tuberculosis** the drug may be employed both internally and locally. Chappell uses the following locally:—

**R.** *Creosote (beechwood)*,

*Oil of gaultheria* ..... f3ij (8 c.c.).

*Liquid petrolatum* ..... f3j (4 c.c.).

*Castor oil* ..... f3iij (12 c.c.).

(The oil of gaultheria and castor oil should first be mixed together, the liquid petrolatum added, then the creosote, and, finally, the solution sterilized by dry heat.)

This solution may either be applied topically, used as a spray, or given in submucous injections. The first method may be relied on, according to Chappell, to relieve the symptoms of primary tuberculous deposits with infiltration and hypertrophy of the mucous membrane, provided there is but little fever and the general condition is good. Cough, soreness, and moderate dysphagia are quickly relieved by sprays of the solution. If, however, the evening temperature is high and the case progressing to active ulceration, a few superficial submucous injections, at intervals of five or six days, under cocaine local anesthesia (generally a 20 per cent. solution of cocaine) should be used as adjuncts. Before ordinary applications or spraying, the interior of the larynx should be well cleansed. An 8 or 10 per cent. solution of cocaine should then be applied, and the spray of creosote used. After this the pyriform sinuses may be filled with creosote solution, and also some of it allowed to drop into the trachea through the opening of a rubber tip drawn over the cannula of the syringe. This will keep the laryngeal surfaces bathed in creosote for a considerable period, and the patient should, if possible, remain perfectly quiet and not talk or swallow for half an hour afterward. Too frequent applications are to be avoided, as undue local irritation will then be produced. In the ulcerative stages sprays of a dram (4 c.c.) of creosote to the ounce (30 c.c.) may be used daily with advantage.

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AND

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## CREOSOTE CARBONATE AND CREOSOTAL. See CREOSOTE.

### CRESOL AND CREOLIN.—

*Cresol* is a coal-tar product, a mixture of the three isomeric cresols (ortho-, meta-, para- cresol), freed from phenol hydrocarbon, oils, and water. It is a colorless or straw-colored liquid which turns a yellowish-brown color when exposed to light for any length of time, and should, therefore, be kept in amber-colored bottles. It resembles phenol in odor and has a specific gravity of 1.038. Cresol is soluble in 60 parts of water, and is easily mixed in all proportions with alcohol, ether, glycerin, alkali hydroxide solutions, and benzene.

*Creolin* is a dark-brown, syrupy liquid derived from soft coal by dry distillation, the carbolic acid being first removed and the residue then treated with soap, caustic soda, or sulphuric acid. It has a tar-like odor. It is soluble in alcohol, ether, or chloroform, and thoroughly mixes with water, forming a milky emulsion.

**PREPARATIONS AND DOSE.**—*Cresol*, which is official, may be given internally in the dose of 1 minim (0.06 c.c.).

*Liquor cresolis compositus*, also official (compound solution of cresol), is composed of 500 parts cresol, 350 parts linseed oil, 80 parts potassium hydroxide, and water, to make 1000 parts. It is used externally.

Creolinum is used externally in the strength of a  $\frac{1}{2}$  to 2 per cent. solution.

**PHYSIOLOGICAL ACTION.**—Cresol is similar in action to phenol, but much less toxic. Its germicidal power is said to be nearly three times as great as that of phenol. In the strength of a 5 per cent. solution it produces some tingling of the skin, which rapidly disappears. It is an irritant to mucous membranes.

Creolin is supposed to be a non-poisonous substitute for phenol, and is used as a disinfectant and deodorizer, but untoward effects have been recorded. It should be employed with care in children.

Case of creolin poisoning in a woman aged 33, wife of a physician, who was being treated for amebic dysentery by irrigations of the colon

with a 2 per cent. solution of creolin. From 1 to 2 quarts (1000 to 2000 c.c.) was injected at each irrigation. After three such irrigations at intervals of eight hours the creolin was reduced to 1 per cent. and the same amount of fluid was used.

About one hour after the fourth injection of the latter strength she was suddenly seized with symptoms of profound collapse, vomiting, cold perspiration, sighing respiration; pulse 140 per minute, small, and thready. The urine passed for the following twenty-four hours smelled of creolin and the same odor was noticed on the breath. This condition was not recovered from till after the lapse of eighteen hours. E. W. Pressly (Phila. Med. Jour., Jan. 20, 1900).

**THERAPEUTICS.**—Cresol may be used both internally and externally for the same purposes as phenol (carbolic acid).

Creolin may be used as a wash for the hands. It is frequently used, in the lying-in state, as a vaginal douche. It may be used advantageously as an antiseptic wash for surgical wounds and as a dressing for fresh wounds. It has been recommended in the treatment of **cystitis** in the female, and is also said to be useful as a nasal douche in **rhinitis** and **nasal ulcers**, and for irrigations in **otorrhea**. It has been employed with good results, in a 1:200 solution, in the treatment of **dysentery** and **colitis**.  
H.

**CRESOL IODIDE.** See EUROPHEN.

**CRETINISM.** See ANIMAL EXTRACTS; also PSYCHOSES; IDIOCY.

**CROTON CHLORAL**, or butyl-chloral hydrate, which occurs as pearly white, trimetric scales, is produced by the addition of water to liquid butyl chloral. It has a pungent odor and a nauseous, acrid taste. Croton chloral is slightly soluble in chloroform; soluble in 90 per cent. alcohol, in 50 parts of water, and in its own weight of glycerin. The drug is not official.

**PREPARATIONS AND DOSE.**

*Butyl-chloral hydras*, B. P. (croton chloral), is given in the dose of from 5 to 20 grains (0.3 to 1.3 Gm.).

**PHYSIOLOGICAL ACTION.**—Croton chloral is similar in its action to chloral hydrate, but has been thought by some to be less depressing to the heart and to possess more analgesic power than that drug.

**THERAPEUTICS.**—Croton chloral may be used for the relief of **headaches** due to eye-strain and is useful in **sleeplessness due to pain**. It has also been used with good results in **facial neuralgia** and **migraine**. H.

**CROTON OIL** is obtained from the *Croton tiglium* Linné, a small tree grown in many parts of India. It is derived from the seeds, which contain from 50 to 60 per cent. of the oil. It is a transparent and viscid liquid having a brownish or pale-yellow color, a peculiar, acrid, persistent taste, a disagreeable odor, and an acid reaction. It is slightly soluble in alcohol, but readily soluble in ether, chloroform, and volatile oils. It should be kept in well-stoppered bottles for at least two years, being of no value when fresh. Croton oil contains a small free proportion of the powerful irritant *crotonoleic acid*. When the oil reaches the intestine, an additional amount of this acid is liberated.

**PREPARATIONS AND DOSE.**—*Oleum tiglii* (croton oil) is given in the dose of 1 minim (0.06 c.c.). The British Pharmacopœia has an official liniment, *linimentum crotonis*, which is used as a counterirritant.

**PHYSIOLOGICAL ACTION.**—Applied locally, croton oil produces irritation and inflammation of the skin and a papulopustular eruption. The pustules may be umbilicated, and leave scars if the oil has been applied undiluted.

Croton oil should not be given in cases of hemorrhoids, in feeble individuals, in children, in peritonitis, in diseases of the stomach and intestines, nor during pregnancy; in the last-named condition it is likely to produce abortion.

Internally, croton oil is an irritant to the gastrointestinal tract, and a powerful purgative, producing copious watery stools

within one to two hours after its ingestion. It is also said to be a hepatic stimulant and alterative. It is diffusible in the blood, and may produce glandular hyperemia, and sometimes an eruption of the skin, which may spread over the entire body.

**POISONING.**—Large doses of croton oil produce nausea, vomiting, severe abdominal pain, violent purging with bloody stools, increased intestinal secretions, collapse, and death. It is less apt to have a toxic action if given in combination with an alkali.

**TREATMENT OF POISONING.**—If free emesis has not been caused by the drug the stomach should be washed out, or copper sulphate given. Demulcent drinks should be used to allay the irritation, and opium to relieve the pain and purging. In case of collapse, cardiac stimulants and external heat are indicated.

**THERAPEUTICS.**—Croton oil is applied locally as a counterirritant in **gout**, **rheumatism**, and **neuralgia**, but not in the undiluted state, as it is liable to cause permanent scars. It has been used, diluted with sweet oil, in **lung** and **laryngeal conditions**, and also in **suppurative tonsillitis**. It may be applied to a small area in obstinate **ringworm**, which has resisted other remedies.

Internally, croton oil is a rapidly acting, drastic cathartic, and is valuable in **comatose conditions**, **cerebral affections**, and **apoplexy**. It may also be used in cases of high arterial pressure and **anasarca**. It is useful in cases of **fecal impaction** which are not due to organic intestinal obstruction, and may also be used in **lead poisoning** after other cathartics have failed. It has been used as a vermifuge in cases of **tapeworm**, but, owing to its violent action, it may simply tear the body of the worm away, the head remaining. H.

**CROUP. — SYNONYMS.**—Catarrhal laryngitis; spasmodic croup; laryngismus stridulus.

**DEFINITION.**—This is an acute inflammation of the larynx and trachea, always associated with a more or less marked catarrh, and non-contagious. It is followed or associated with

a trachitis or a bronchitis. The most characteristic symptom is the croupy cough, which may also be described as barking, crowing, or metallic in character.

Croup is one of the most common of the diseases of early childhood; the most common time of its occurrence is the changeable weather of Spring and Fall, though it is found at any season of the year. The attack may be mild or severe, associated with much catarrh or spasmodic in type. At times the physician has difficulty in distinguishing this condition from true pseudo-membranous croup (laryngeal diphtheria) but careful study of the case soon clears it up

The writer has noted that syphilitic disease of the throat may present the same picture as membranous croup, as observed in 2 small boys in 1 family. Diphtheria was somewhat prevalent and the croupy breathing, inflammation in the throat, and pseudomembranous patches on the tonsils imposed the diagnosis of diphtheria. Their young and healthy parents had had a maid servant for a year, whom they had dismissed about 2 weeks before, and who turned out to be a patient of the writer's in a most highly contagious stage of syphilis. He then examined the third child in the family and found a well-defined roseola on the chest. F. Arocena (*Revista Medica del Uruguay*, Sept., 1920).

**SYMPTOMS.**—In rare instances the onset of catarrhal croup is sudden, with no premonitory symptoms. More commonly the child has a slight cough and coryza and becomes hoarse during the afternoon and perhaps feverish in the evening. Late in the evening the cough becomes loud, dry, and hoarse, its characteristics being peculiar and distinctive. In the great majority of cases this occurs between the hours of 9 and 12.

The child wakes suddenly with a barking cough and begins to struggle for breath. He frequently becomes alarmed at his inability to breathe, and his fright adds to the severity of the symptoms. In attacks of ordinary severity the respiration is loud and noisy; the voice is hoarse, but rarely lost; the dyspnea is sometimes extreme and the respiration so noisy that it can be heard in an adjoining room. The loud, metallic cough is very different from the stridulous, suppressed cough of a well-developed case of pseudomembranous laryngitis. There may be recession of the various thoracic spaces on inspiration. The temperature is usually somewhat elevated, but rarely reaches 102 degrees. The lips and nails frequently assume a purplish hue, but are rarely cyanotic. There is often a discharge from the nose, and the eyes are sometimes congested and watery, conditions not usually present in pseudomembranous croup. After two or three hours the symptoms usually subside. Occasionally they appear in less severe form later in the night, but, as a rule, all urgency is passed by early morning. In some instances the child is almost as well as usual during the following forenoon, and shows but little evidence of the experiences of the night. The attack, however, is usually repeated during the following night, and may recur for several nights, becoming less severe with each succeeding attack. In my experience, however, this freedom from symptoms on the following day is extremely rare. More commonly the child continues to be feverish and has a troublesome cough, although it may not be croupy in character. In the damp climate of New York and vicinity an attack of croup, as a rule, is but the initial symptom of a bronchial or laryngeal

catarrh, which requires several days or a week or more to run its course. Attacks more mild in form, but similar in nature, are of frequent occurrence and must be considered as simply mild attacks of croup. In other instances the attack appears to be really one of bronchitis, with a dry and croupy cough at night.

The writer establishes the diagnosis by means of the stethoscope. This is placed over the upper part of the larynx, which is behind the thyroid cartilage, and slightly to the left of the median line, and then over the suprasternal fossa in the median line. Over the normal larynx of a child a supping sound is heard in inspiration and a similar, although somewhat longer, sound in expiration. In pseudocroup, an indistinct tone similar to that made in pronouncing the letter M is heard over the thyroid cartilage in inspiration, and a long drawn out supping sound is heard in expiration. A. Levinson (Münch. med. Woch., Feb. 2, 1915).

#### DIFFERENTIAL DIAGNOSIS.

—In typical cases of catarrhal croup the diagnosis is evident at a glance. The sudden onset during the early hours of the night; the immediate development of extreme symptoms; the loud, metallic cough; the noisy respiration, the terror, and the rapidity with which the attack subsides all combine to form a typical clinical picture. In less marked cases, however, the diagnosis is somewhat difficult.

Catarrhal croup should be distinguished from acute catarrhal laryngitis. The latter disease may be primary, secondary to the infectious diseases, or traumatic. The lesions are found chiefly in the mucosa and lymphoid tissue of the subglottic region, and in severe cases they may be so pronounced as to cause laryngeal stenosis. This disease is frequently a complication of bronchitis. It

is marked by hoarseness and a frequent, harassing, metallic cough, which always becomes worse at night and is usually aggravated by lying down. The milder and more common cases are usually seen in children between 1 and 6 years. Although extremely annoying, they are rarely dangerous or fatal. A severe type is sometimes seen, however, which may prove fatal. In this type the temperature is high; the voice is metallic and may be suppressed; laryngeal stenosis may become so great as to demand intubation. This disease is differentiated from pseudomembranous laryngitis with the greatest difficulty.

The disease may be mistaken for pseudomembranous croup, laryngismus stridulus, and even pneumonia. The presence of foreign bodies in the larynx must be excluded, as well as retropharyngeal abscess. The sudden onset, remission of symptoms, hoarseness without loss of voice; loud, metallic cough, with little or no stridor, and the response to treatment usually suffice to distinguish catarrhal croup from pseudomembranous croup, with its insidious onset; slower, but more steady and unremitting course; suppressed voice and cough, increasing cyanosis, embarrassed expiration, and characteristic stridor. Laryngismus stridulus is a disease of early infancy. The symptoms occur in paroxysms, which are usually repeated many times a day and occur at no definite hour. They are unaccompanied by any evidences of catarrh. The disease invariably occurs in rachitic infants, and is a frequent accompaniment of tetany or general convulsions.

I have twice been called in consultation to find bronchopneumonia in young children in which, when dry, difficult cough combined with an unusual degree

of expiratory dyspnea had been mistaken for croup.

**ETIOLOGY.**—Age is an important predisposing cause of the disease, which is most common between 2 and 5 years. It is very rare under 1 year and over 8. It may occur, however, at any time until adolescence, and I have seen a typical case in an adult.

Heredity is also an important predisposing cause, the disease occurring with especial frequency in some families. Enlarged tonsils and adenoid growths also predispose to croup. It is sometimes brought on, apparently, by atmospheric conditions, as it is not uncommon to see several cases at about the same time. It cannot, however, be called an epidemic disease. Exposure to cold is undoubtedly the most important and exciting cause. Excessive use of the voice in damp and cold weather is also a frequent cause. Indigestion often precipitates an attack in a sensitive child.

**PATHOLOGY.**—The lesions of catarrhal croup are found chiefly above the vocal cords and are those common to all catarrhal inflammations of the mucous surfaces. The spasmodic symptoms are due chiefly to spasm of the adductors. The disease may appear primarily in the larynx, or it may extend from the nasopharynx downward, or, more rarely, from the trachea upward.

**PROGNOSIS.**—Ordinary types of catarrhal croup are never fatal. In very rare instances in which the catarrhal element predominates and is very severe, the prognosis may be grave. In other words, catarrhal croup is rarely or never fatal, while severe catarrhal laryngitis with spasm may be dangerous.

**TREATMENT.**—Preventive treatment consists in the removal of all evident exciting causes, such as enlarged tonsils and adenoid growths, and in the

relief of indigestion. **Exercise in the open air** is important, but the child must be properly clad, and all exposure should be avoided. Screaming and excessive use of the voice while at play during damp and stormy weather should be prohibited. Anemic and delicate children should receive proper constitutional treatment. Relief of the paroxysms may be sought by external application and medical treatment. **Turpentine stupes** are thus applied: 1 part of turpentine to 3 parts of olive oil is painted over the neck and this is covered by a flannel wrung out in boiling water, over which is placed a dry piece of flannel. As soon as cool, another hot piece is applied and with every third change the neck is again painted with the turpentine mixture. This is the most effective remedy for the acute paroxysm. A large, **hot poultice over the throat and chest** will do much to relax the spasm. A large bath **sponge saturated with water** as hot as the child can bear, and **applied to the throat**, is almost as effective as a poultice and is more readily managed. Vigorous rubbing with hot, **camphorated oil** is also efficacious. The use of the **croup kettle and tent** will sometimes prove more effectual than any other measure. The steam seems to be the effective agent, but is somewhat aided by the addition of volatile substances, particularly **creosote, compound tincture of benzoin, or oil of eucalyptus**, one dram (4 Gm.) to the quart (1000 c.c.) of boiling water.

Among drugs, **ippecac, opium, and antipyrin** have proved most efficacious in my experience. If there is acute indigestion, emesis through the use of ippecac will sometimes check the attack permanently. In

other cases emesis is not usually followed by complete and permanent relief. The wine of ipecac is more prompt and effective in its action than the syrup. Opium I have found the most efficacious drug in checking spasm. One full dose, adapted to the age of the child, may be given, but the ipecac may be repeated several times. **Antipyrin** is an extremely effective drug in most cases, but sometimes fails to give material relief. The best results are seen from its use when the catarrhal element is slight and the spasmodic element marked. It is a comparatively safe drug for use among children. Two grains (0.13 Gm.) may be given at 2 years, half the dose to be repeated in one hour if necessary. My most common plan of treating the paroxysm is as follows: After evacuation of the stomach and bowels, in case of indigestion or constipation, a **hot sponge** or **poultice** is applied to the **throat** and a full dose of **antipyrin** given. If no relief is manifest in forty-five minutes, a second dose is given, while a few 10-drop (0.6 c.c.) doses of wine of **ipecac** are given in the interval.

The writer recommends a method which he has tested for four years with uniform success, having treated and brilliantly cured 20 cases of true croup. He employs **calomel** and **apomorphine**, as follows:

**R Calomel** ..... gr. iij (0.2 Gm.).  
**Sugar** ..... ʒss (2 Gm.).

Make eight powders. One powder every two hours.

**R Apomorphine hydrochlorid** ..... gr. ¼ (0.01 Gm.).  
**Distilled water** . ʒiiss (105 c.c.).  
**Dilute hydrochloric acid** ..... gtt. ij (0.12 c.c.).  
**Syrup** ..... ʒij (8 Gm.).

Teaspoonful to dessertspoonful every two hours.

The two remedies are given alternately, so that the patient gets calomel one hour and apomorphine the next. For children under 2 years, the dose of calomel is reduced to about ½ grain (0.01 Gm.). Both prescriptions may be repeated, and in the author's cases more than two repetitions were never required. The calomel should be partially discontinued as soon as amelioration is noted, lest untoward results appear. The apomorphine may be continued longer. The sooner this treatment is begun, the better. L. Bayer (Therap. Monats., Bd. xvi, No. 4, 1902).

**Creosote carbonate** is sometimes quite effective. It may be given in 5-grain doses.

In all cases of croup occurring after measles, **diphtheria antitoxin** should be given, according to the writer, even though the bacteriological examination is negative. Antitoxin should also be given in other cases in which diphtheria is suspected. **Intubation** is often indispensable. E. Suñer (Jahrb. f. Kinderheilk., vol. xxx, Nu. 6, 1914).

A mixture that I have always found to be effective during the acute stage and particularly for the following days is:

**R Sodii bicarb.** .... gr. xlviii (3.3 Gm.).  
**Syr. ipecac** ..... ʒj (4 c.c.).  
**Spts. atheris nitrosi** ..... ʒiij (12 c.c.).  
**Glycerini** ..... ʒv (20 c.c.).  
**Liq. potassii citratis** . . . q. s. ad. ʒiij (90 c.c.).

Sig. Teaspoonful every 2 to 3 hours, or during the acute stage every hour; this I believe is better than the brown mixture as it does not upset the digestion and does control the paroxysm, in most cases to a marked degree.

**Antipyrin** is very effective in preventing recurrence on the following nights. Two grains (0.13 Gm.) administered in the afternoon and again in the evening will alone frequently prevent the attack. It can, however,

be given in addition to the usual cough mixture.

The depressing action of antipyrin should always be borne in mind, and its action should, therefore, be carefully watched, lest it affect the heart unfavorably. EDITORS.

To prevent the immediate recurrence of the attack there is no drug like **antipyrin**. It may be given in doses of 2 grains (0.13 Gm.) to a child of 2 years, and repeated in two hours if necessary. When this drug is used the heart must be watched very carefully. On the following day the child must be kept in a well-ventilated and sunny room, with a temperature about 72° F. (22.2° C.). Stimulating expectorants, such as **ammonium chloride** or **carbonate**, should be given. If the child is of a nervous disposition **potassium bromide** is called for. The nose and throat should be cleansed with **Dobell's solution**, followed by a **spray of liquid petrolatum** to which has been added 1 per cent. of **menthol** or **thymol**. The bowels must be kept open by broken doses of **calomel** if necessary. I. W. Brewer (N. Y. Med. Jour., Nov. 3, 1906).

## PSEUDO MEMBRANOUS CROUP.

The etiology and nature of pseudomembranous laryngitis was for years the subject of much discussion. The question has at last been settled by the bacteriologist, who has demonstrated that, in the great majority of cases, the disease is diphtheritic. It is equally demonstrated, also, that a certain proportion of cases are not diphtheritic.

Of 286 cases, reported by Park and Beebe, the Klebs-Löffler bacillus was present in 229. In the remaining 57 cases it was not present, but in 17 the examination was not satisfactory. The observations of recent years have shown that a pseudomembrane developing primarily in the larynx is almost invariably associated with the Klebs-Löffler ba-

cillus; that is, it is true diphtheria. Pseudomembranous inflammation of the larynx secondary to diphtheritic inflammation of the pharynx is invariably true diphtheria. A pseudomembrane developing in the larynx secondarily to the pseudomembranes which develop during the course of the infectious diseases is commonly pseudodiphtheria. Such pseudomembranes are associated with microorganisms other than the Klebs-Löffler bacillus, generally the streptococcus.

Whatever the cause of the disease, whether bacillus or streptococcus, it manifests itself simply as a pseudomembranous laryngitis, stenosis being the important symptom.

**SYMPTOMS.**—As the disease is so frequently diphtheritic in nature, it will be considered in detail in the section on diphtheria. Owing to the slow absorption of toxins by the laryngeal mucous membrane and the comparatively short course of the disease when confined to the larynx, the constitutional symptoms of diphtheria are slight. Hence, croup pursues practically the same course, whether due to diphtheria or pseudodiphtheria. It is impossible from clinical evidence alone to determine whether the disease is true or false diphtheria. As it is true diphtheria in a very large proportion of cases, the only safe rule in practice is to consider every case of croup to be diphtheritic and to use precautions accordingly.

During the winter of 1906 the writer encountered 9 cases of membranous croup independent of the diphtheria bacillus in his diphtheria wards. While the clinical picture was that of membranous croup, three to seven bacteriological examinations of the false membrane failed to disclose the diphtheria bacillus in a single instance. There were only 5 immediate deaths in the group of 15

cases, but 2 of the patients succumbed later to complications and another required intubation permanently. Those patients who recovered were ill only a few days. None of the patients had any symptoms of coryza, but the temperature was much higher than in diphtheria, and the glands in the neck were not swollen or tender. The infection seems to affect the entire respiratory tract from the start, so that the symptoms on the part of bronchi and lungs were prominent from the first. The entire larynx and lungs were involved in the 5 cases in which autopsy was possible. The false membranes extended to the bifurcation and even into the large bronchi, while the lungs were congested, with foci of bronchopneumonia. Wherever the tube had rubbed there was ulceration. Unless there is marked relief from the expulsion of the false membranes early, the patient does not seem to be relieved by intubation or the injection of antidiphtheria antitoxin; the temperature remains high and pulmonary symptoms predominate. M. Jacod (*Semaine méd.*, Oct. 23, 1907).

**PATHOLOGY.**—In some cases the anterior portion of the larynx alone is involved by pseudomembrane. In other cases the whole mucous membrane of the larynx is covered. In many instances the membrane does not pass below the larynx. In both true and pseudo-diphtheria the membrane is but one element in the production of stenosis, edema and swelling of the tissue underneath the pseudomembrane being an important contributing cause.

**PROGNOSIS.**—Unlike pseudodiphtheria of the pharynx, pseudodiphtheria of the larynx is almost equally fatal with true diphtheria, as it causes death by mechanically obstructing respiration. Until a few years ago the age of the infant was the most important factor in

prognosis, the younger the child, the more fatal being the disease.

Age is still a very important factor, but prompt treatment with antitoxin must be considered of far greater importance in modifying the prognosis.

**TREATMENT.**—The efficacy of the antitoxin treatment of diphtheria has been too fully established to permit of doubt or argument. It is more effective in croup than in any other form of diphtheria. An injection should be given on a clinical diagnosis without waiting for a bacteriological examination. From 15,000 to 24,000 units of antitoxin should be injected into the thigh muscles. Its early use will, in a large proportion of cases, prevent the necessity of operation. Next to the antitoxin treatment, **calomel fumigations** have proved most efficacious.

Eight cases of severe membranous croup in which it proved impossible to detect the presence of the Löffler bacillus. Streptococci, influenza bacilli, and diplococci were found, and symptoms of **rippe** accompanied or preceded the manifestations of croup, the maximum phase being reached about the fourth day. **Intubation** was required in some of his cases and he never failed to inject **antidiphtheritic serum**; it produced an unmistakably favorable effect, supplemented by hot **mustard foot-baths** and **inhalation of steam**. Istomin (*Med. Oboz.*, vol. lxi, No. 8, 1905).

**Turpentine stupes** (method, see under Catarrhal Croup), will in many cases give relief and intubation will not be necessary, but intubation should be prompt when indicated (see DIPHThERIA and INTUBATION).

Among the other measures recommended, **turpentine** and **hydrochlorate of ammonia** hold a prominent place, but the measures already outlined are to be preferred. Increased



experience has led most practitioners to the use of two measures only in the treatment of membranous croup—antitoxin and intubation.

Many remarkable cures have been reported by various writers, commencing with Harder, in 1821, by means of the **water treatment** of membranous croup, the aim being to induce powerful revulsion by sudden **cold douches**. Winternitz applied the method thus: The body was rubbed with sponges dripping with water at 10° C. (50° F.) for 6 minutes. While this was being done the head and back of the neck were repeatedly doused with cold water from a height, with packs in the interim, until pulse and temperature were nearly or quite normal. Bartels, of Kiel, has applied the water treatment in a number of severe cases with great benefit, as an adjuvant to **intubation** and **tracheotomy**. If the temperature is low, the child is previously placed in a warm bath. Sadger (*Archiv. f. Kinderheilkunde*, Bd. xlv, Nu. 1, 2, 1907).

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**CRYOSCOPY.**—This word comes from the Greek "kryos," meaning frost, and "skopeo," meaning to see. The freezing point of a solution is obtained and compared to a solvent the freezing point of which is zero. There being a direct relationship between the molecular concentration and the freezing point of a solution, Dreser in 1892 first observed that the molecular concentration of the blood was changed in certain conditions, particularly in diseases of the kidneys. He concluded, therefore, that the freezing point of the blood could be of service as a clinical method. His method proved too complicated, however, and we owe to von Koranyi (1897) its development.

One must go back to the physico-chemical researchs of Van t' Hoff to understand this method, which was introduced into clinical medicine by

Dreser and von Koranyi. According to the law of Van t' Hoff, the osmotic pressure of a solution is, like that of a gas, dependent on the number of dissolved molecules and is as large as that of the corresponding gas. Hence the osmotic pressure is dependent on the molecular concentration of a solution. Substances of like osmotic pressure have like freezing points. Inasmuch as certain substances exist in solution in the form of electrically charged ions, the latter influence the osmotic pressure in the same way as molecules. From the above facts it can be seen that the determination of the freezing point of a liquid furnishes an indication of its degree of concentration. Moreover, since the electrical conductivity of a solution is dependent on the number and character of its ions, the determination of their conductivity would serve as one of the methods of the determination of its freezing point. Only the crystalloid bodies, such as salts, acids, and bases, influence the osmotic pressure, the molecular concentration, and the freezing point of a solution, while the colloids, such as albumin, dextrin, gelatin, and other bodies, have almost no effect upon it. For example, a proteid molecule with a molecular weight of 14,000, taking up 14,000 times the space of a molecule of oxygen, has only the same influence on the osmotic pressure of a solution as the latter. The application of these principles of physical chemistry is of eminent value in the diagnosis of the different degrees of renal insufficiency. If the capacity of the kidneys be impaired, so that they can no longer normally separate the dissolved substances from the solutions, namely, the blood and lymph, that flow through them, then there occur marked changes in the osmotic pressure; hence in the freezing point of these solutions. Renal insufficiency indicates a retention in the body of the products of metabolism. The constancy of the molecular concentration of the blood indicates that the

action of the kidneys which decreases this concentration is neutralized by the wear and tear of the tissues which tend to increase it. In cryoscopic experiments, the normal freezing point of dogs' blood,  $0.56^{\circ}\text{C}$ ., has been taken as a physiological standard. Bilateral nephrectomy performed on a dog causes a retention of metabolic products, a rise in molecular concentration, and a lowering in the freezing point of the blood. The resection of one kidney does not lead to retention, if the other kidney be intact. If the latter be injured in any way retention occurs. The effect of renal poisons is generally bilateral and leads to a lowering of the freezing point of the blood. This is markedly seen in poisoning by cantharides, which affects mainly the blood-vessels of the kidneys, and in the toxic action of aloin, which affects all the renal tissues. Potassium chromate causes the same effect by acting toxically upon the tubular apparatus of the kidneys, while poisoning with potassium oxalate leads to the same result by the production of artificial infarcts. Not only to the physician, but also to the surgeon, the cryoscopy of the blood and urine is of value. According to Lindemann, it is of practical importance in the differential diagnosis between simple albuminuria and that due to inflammatory changes in the kidney. H. Roeder (*Medical News*; *Archiv f. Kinderheilkunde*, May, 1902).

**TECHNIQUE.**—The freezing point of the blood is designated by the Greek letter delta ( $\delta$ ), and is normally  $-0.56^{\circ}\text{C}$ . It is determined by the Beckmann apparatus. This consists of a glass cylinder and a delicate thermometer. The thermometer is graduated in 100 parts, each part being subdivided into 100 degrees.

About 20 c.c. ( $\frac{3}{8}$  ounce) of blood is removed from a vein of the arm, preferably the median basilic, under aseptic conditions. This is received in a clean, closed vessel and defibrinated by shaking with a platinum ring, and then put into the cylinder of the Beckmann apparatus. The thermometer is placed in the glass cylin-

der and the blood constantly agitated by means of a platinum stirrer. The whole apparatus is placed in a freezing solution at  $-4^{\circ}\text{C}$ . and the blood constantly stirred until it coagulates. Heat is then liberated, causing the mercury to rise to a certain point where it remains for a time and then falls; this is known as the physical freezing point. The freezing point of distilled water is now determined in the same manner and by the same apparatus. The freezing point of the blood being then subtracted from the freezing point of the water, the result shows how much lower the freezing point of the blood is than that of water. That of the blood, as stated above, is normally  $-0.56^{\circ}\text{C}$ .

The lowest limit to which the blood freezing point may drop, without indicating renal insufficiency, is  $0.58^{\circ}\text{C}$ ., while a figure of  $0.59^{\circ}\text{C}$ . is already significant of inadequacy of both kidneys. The causes of such insufficiency may be various; for example, there is a reflex insufficiency due simply to pain in the one organ, while the other is perfectly healthy, and certain mechanical conditions, like the presence of large abdominal tumors, whether renal or not in origin, may have a similar effect. Therefore, the blood freezing point is to be taken as an index of disease of both kidneys only when such extraneous factors can be excluded. The conflicting figures which have been published by other observers the writer attributes to the lack of certain precautions which it is essential to observe. Chief among these is the employment of sufficiently large quantities of blood; at least 10 to 15 c.c. ( $\frac{1}{8}$  to  $\frac{1}{2}$  ounce) are required, but, as the freezing point of blood and serum are the same, the troublesome separation of the serum is unnecessary and the attendant waste of material is saved. Another point not to be neglected lies in the elimination of the carbonic acid, which is always present in excess, no matter in what manner the blood is obtained, and as it is variable in amount introduces an inconstant factor into the calculations that must be obviated by a prelimi-

nary saturation with oxygen either directly or simply by agitation with air. By the use of Beckmann's apparatus the determination may be quickly made and is accurate to  $0.01^{\circ}$  C., which is all that is required. A. von Koranyi (Berl. klin. Woch., April 22-29, 1901).

The freezing point of blood varies normally, according to the changes occurring as the result of exercise, baths, meals, etc.

The writer found that, after a test meal consisting of bread, the freezing point of the gastric contents is at first very low, but rises considerably during the succeeding hour and a half. After ingestion of meat, on the contrary, the freezing point is at first very high, then gradually falls. The author concludes that, whatever material is ingested, the freezing point tends gradually to a certain level, which is  $0.35^{\circ}$  C. L. Meunier (Presse méd., May 23, 1914).

The freezing point of urine is determined in the same way as that of blood. It varies when the kidneys are healthy between  $0.87^{\circ}$  and  $2.43^{\circ}$  C., and is designated by the sign "Δ." The urine of each kidney must be collected separately by ureteral catheterization.

It has been noticed, in certain diseases of the kidneys in which uremic symptoms developed, that the latter corresponded with a lowered cryoscopic blood index, but Schoenborn noticed, in a series of 88 cases, that the freezing point remained about normal, while Englemann found, in a study of 36 cases, the freezing point to average  $-0.664^{\circ}$  C.

In disease of one kidney the freezing point of the blood remains normal if the other kidney is healthy, while in disease of both kidneys it has been found to be lowered. In nephritis, the insufficiency of the kidneys increases as the freezing point becomes lower. In all cyanotic conditions the freezing point has been found lower than normal owing to the increased proportion of  $\text{CO}_2$ .

One is enabled by cryoscopy to determine the existence of renal disease as opposed to bladder disease, or the existence of renal disease in a case of heart disease, or the ability

of the heart to withstand the strain of exercise (von Koranyi). It also has a medicolegal value in the case of death from drowning. Whether it is an absolute test remains to be seen. Cryoscopy does not, any more than any other means of diagnosis, enable one to say that a kidney must or must not be removed. It is futile to expect any mode of examination of the urine or blood to give an infallible opinion on such a matter. O. C. Gruner (Med. Chronicle, Sept., 1906).

The freezing point of urine rises in conditions in which the function of the kidneys is disturbed and is of most value as a diagnostic measure when only one kidney is diseased, the urine from each kidney being collected separately by ureteral catheterization. The freezing point of the urine from the affected kidney is below  $0.87^{\circ}$  C.

Cryoscopy of blood, done correctly, gives a point of about  $0.56^{\circ}$  C. below zero in the presence of healthy kidneys. This point is not materially altered through unilateral kidney lesions, provided that the other organ is anatomically and functionally intact. A lowering of the blood-point to  $0.52$  and lower is generally found in anemia or cachectic individuals with otherwise healthy kidneys. A rise to  $0.60$  and above should be interpreted as a danger signal of derangement of renal function and should indicate caution against radical operative procedures. In the hands of a critical observer, cryoscopy of blood is a valuable test for the estimation of absolute or total renal function, especially when estimation of relative function, through ureteral catheterization, is not feasible. M. Krotoszyner and C. W. Kartman (Jour. Amer. Med. Assoc., Jan. 18, 1913). H.

**CRYOTHERAPY.** See ETHER, ETHYL CHLORIDE, LIQUID AIR, REFRIGERATION, etc.

**CRYPTORCHIDISM.** See PENIS AND TESTICLES, DISEASES OF: UNDESCENDED TESTICLE.

**CRYSTALLINE LENS, DISEASES OF.—ANOMALIES OF POSITION.**—Anomalies of position are always the result of changes in the zonula of Zinn.

It is ordinarily supposed that the crystalline lens occupies the ideal position represented in the textbooks, that the axis of the lens passes through the center of the cornea, and that the vertical and the horizontal diameters are exactly at right angles to its axis. Moreover, we usually take it for granted that during the act of accommodation the two surfaces of the lens become more convex, always in an equal and regular manner. Most of these assumptions are not warranted, at least not in the majority of what we call normal eyes. This conclusion was reached after a study of (1) the appliance for viewing the two surfaces of the lens, or rather the reflections from them; (2) formulas for calculating the position of the lens, and the changes which its surfaces undergo during accommodation; (3) what these calculations show as to the position of the lens and its changes under the action of the ciliary muscle.

As to the clinical importance of abnormal positions or changes in the lens, it is evident that any displacement or irregularities in the surfaces of the lens will produce a certain amount of astigmatism. This was long ago recognized as lenticular astigmatism. While it is true that the astigmatism produced by displacement is usually only of a slight degree, probably not exceeding 0.75 diopter in most cases, the important point is that displacement or especially the varied and unequal changes in the surface call for correspondingly varied and unequal demands upon different portions of the ciliary muscles. As to which irregularities in the position or in the changes of the lens correspond to certain clinical symptoms, the observations thus far are too few and unreliable to warrant any very definite conclusions.

We need phacometric studies of the changes which take place in those images during the act of accommodation in normal and in abnormal eyes. It seems probable that our views will change concerning the phacometer; some practitioners are still living who can remember when the ophthalmoscope was a vain novelty. Lucien Howe (*Ophthalmology*, Jan., 1912).

**CLASSIFICATION.**—Cases of dislocation of the lens are commonly divided into two groups: in one of which the lens has completely left the fossa patellaris (luxation, or complete dislocation), while in the other it still remains partly within this cavity (subluxation, or partial dislocation); but as it is usually only a matter of time for cases in the latter group to find their way into the former, this distinction only marks a stage in the history of the case.

A more convenient and comprehensive classification can be made on an etiological basis.

Dislocations of the lens are either *congenital* (ectopia lentis) or *acquired*.

The latter group may be thus divided:—

1. Traumatic cases, in which the lesion varies in degree: (a) There may be a partial displacement, the lens being caused to rotate on its axis, or pushed sideways, thus assuming an oblique position, or a position with its edge in the pupil; or it may be displaced sideways and rotated. (b) It may be completely dislocated into the anterior chamber. (c) It may be completely dislocated into the vitreous chamber. (d) It may pass through a rent in the sclerotic, and lie under the unbroken conjunctiva: subconjunctival dislocation. (e) It may pass through a rent in the conjunctiva. (f) It has been found beneath Tenon's capsule.

2. The lens may escape from the eye at the moment of rupture of the floor of a large corneal ulcer: a more common incident in the cases of ophthalmia neonatorum than in any other form of disease.

3. It may be dragged out of position by iridic adhesions when the iris is stretched or rendered tense by the occurrence of peripheral staphyloma.

4. It may be pushed out of position by intraocular tumors.

5. Its displacement may be spontaneous.

Four types of non-traumatic lens displacement are illustrated by cases reported by the writer. The first group includes congenital cases in which treatment is sought, either to improve existing vision or to prevent the possibility of future trouble. If, in these cases, treatment by correcting lenses will not suffice, iridectomy, discission, or extraction may be considered. The age of the patient, the degree of displacement, the size of the lens, and the amount of vision obtainable, with or without correcting lenses, after complete mydriasis, enables us to decide for or against **iridectomy**. Since congenital displacement is almost always upward, the iris excision would be below, and the possibility of future downward displacement occurring and vitiating the result ought to be thought of. The family history as regards this tendency should be inquired after. **Discission** is proper when the patient is under 25 years of age and finds his vision insufficient. It may, however, be impracticable with a very movable lens. **Extraction** is naturally resorted to when operation is required and the other two cannot be done. It is especially to be practised in patients over 35 years of age. Group two includes cases in which the lens is not only displaced, but also opaque from intraocular disease, and discission or extraction is the choice of opera-

tions. After the age of 25, the author prefers extraction, preceded by iridectomy. Before that age, and if the tendency to active inflammation is not too great, the **needling** operation may be preferred. The writer advises not to try to better a fair result by division of secondary membranous cataract when there are vitreous opacities that may be increased thereby. It is best not to promise too much from operation in cases of this group. Group three includes cases of lens displacement complicated by acute glaucoma, and here iridectomy, alone or combined with extraction, must be considered. Which of these is best depends on the position of the lens, its liability to be retracted again into the hyaloid fossa, whether it has been injured in the iridectomy or not, and its previous opacity. For the cataractous and displaced lenses following acute glaucoma, which comprise group four, only extraction is to be considered for restoration of sight, and, on account of the risk of intraocular hemorrhage, the prognosis must be a guarded one. The writer advises in these cases a preliminary iridectomy, and, if the intraocular tension still keeps high, **sclerotomy** may be done before attempting extraction of the cataractous lens. L. D. Brose (Jour. Amer. Med. Assoc., Aug. 8, 1908).

Ectopia lentis seems to depend upon imperfect or incomplete development of the zonula, and, as this developmental failure occurs especially along the line where closure of the ocular fissure takes place, the more perfectly developed fibers at the upper part drag the lens in their direction. Consequently congenital displacements are almost always directly or obliquely upward. They are also usually symmetrical, and are not infrequently accompanied by coloboma of the lens, which, moreover, is apt to be undersized and thicker than normal.

In accordance with the above theory, dislocation of the lens is occasionally

associated with coloboma of the iris, ciliary body, and choroid.

A case is on record in which the coloboma of the iris was upward, there being a subluxation of the lens downward.

Although at first partial, congenital dislocation often becomes complete, through degeneration and stretching of the fibers of the zonula; the lens then becomes movable to a degree which varies greatly not only in the vitreous humor itself, but it may even pass backward and forward through the pupil: a condition termed by Heyman "spontaneous motility of the lens."

So long as a congenital dislocation of the lens remains incomplete, there is no special tendency toward the formation of cataract; but when it becomes complete, and freely movable in the eye, the impairment of nutrition thereby involved leads more or less rapidly to its opacification. Occasionally a lens dislocated into the vitreous will remain clear for years.

The writer questions the theories offered of the causes of the absorption of the lens after needling operations and gives its chemical composition according to the analyses of Haliburton and Neumeister. These show that it contains 35 per cent. of protein, the highest percentage of any tissue of the body, and, if they are correct, make it hard to accept the theories. He gives details of experiments which seem to prove that there is an autolysis of the broken-up fibers of the lens, but he cannot answer some of the questions it suggests. Whether this is increased by the action of some specific enzyme in the aqueous or not, or, if there is a ferment, what its source is, he admits, is difficult to say. C. A. Clapp (*Jour. Amer. Med. Assoc.*, March 18, 1911).

Of all cases of dislocation of the lens, those of traumatic origin are, by far, the

commonest. The traumatism usually consists of a blow by a blunt instrument, such as the fist or a stone, upon the eyeball; but concussion from a blow upon the side of the head may have the same result. Dislocation is more apt to occur when the vitreous is fluid: a condition which may be accompanied by degenerative changes in the zonula, in old age, and in sclerectasia anterior.

Traumatic dislocations present every variety and degree, from the slightest lateral displacement or rotation to complete expulsion of the lens from the eyeball.

The traumatism that is the immediate occasion of the displacement is often the cause of other ocular lesions, which may, for a time, obscure the diagnosis, and render prognosis more uncertain than would otherwise be the case. The dislocation of the lens may, indeed, be by no means the most important lesion produced. It is common to find hemorrhage in the anterior chamber immediately after the injury, the full extent of which cannot be ascertained until absorption has taken place, or we may find dilatation and immobility of the pupil, hemorrhage into the vitreous, or rupture of the choroid, and—especially in myopic eyes—detachment of the retina. In greater degrees of violence the eyeball may be ruptured, usually in the sclera just behind and concentrically with the sclerocorneal junction, and through this rupture the lens—with the iris, choroid, retina, and vitreous—may escape.

Case of a young man whose lens has contained a foreign body for the past seven years, with retention of full vision and full functional activity of the eye. The foreign body entered the lens through a small wound at the lower nasal part of the cornea. It can be seen in the lens

as a dark, glistening particle, a little to the supratemporal side and slightly posterior to the equator. It was thought to be a piece of steel, irregular in shape and about 2 mm. in its largest diameter, a chip from using a chisel on a piece of steel. There was almost no reaction and the wound healed promptly. There were two attacks of what seemed to be conjunctivitis during the four months following the injury. There were no further ocular symptoms, and the lens has remained clear. Lewis (Med. Record, Aug. 6, 1904).

Case of a woman of 35 who, while attempting to loosen the lid of a box by pounding the head of a hatchet with a hammer, received an injury to the left eye. Within twenty-four hours of the time of the accident a delicate linear scar was visible at the junction of the upper and middle thirds of the cornea, opposite the upper pupillary margin, a punctured iris, and a swollen and partially opaque lens. A skiagraph located the steel partly in the lens and partly in the vitreous, lying horizontally and about 4 mm. in length. The eye was moderately congested, sensitive to light, and vision was reduced to the perception of large moving objects. Under antiseptic precautions and cocaine anesthesia removal was safely accomplished. The operation was divided into two stages: First, the magnet was cautiously approached toward the cornea in the line with the presumed passage of the body, until it was three-fourths of an inch distant, when the steel fragment was raised from its bed in the lens and drawn, accompanied by lens matter, into the anterior chamber. The current was cut off and the steel dropped into the bottom of the chamber. Second, the cornea was opened in as near as possible the line of the scar, the blunt tip of the magnet applied to the opening, the current turned on, and the steel extracted. The greater part of the cataractous lens was expressed through the corneal cut without loss of vitreous and the eye was

bandaged. Two days later the patient was allowed to go to her home. According to the last report of her attending physician, she had a low grade of iritis, probably induced by the traumatism and by the retention in the anterior chamber of a small mass of lens matter. Hansell (Amer. Med., June, 1906).

Spontaneous dislocation of the lens may take place while its transparency remains unimpaired, but it seems to occur more commonly when the lens has become cataractous, and more especially when the cataract has been allowed to progress to a condition of hypermaturity (Morgagnian cataract). Although in some cases the displacement occurs without any evident immediate exciting cause, in many the acts of coughing or sneezing determine it. Gunn, in 1895, reported a case of quite spontaneous symmetrical displacement of the lenses in a man aged 76. Three months before vision failed a recorded examination showed it to be  $\frac{1}{2}$  in each eye, with refraction corrected. Three months after failure both lenses were found displaced downward, their upper edges being visible just within the margin of the dilated pupil, one lens still remaining clear, the other having become opaque. Corrected vision in each eye,  $\frac{1}{2}$ . Fundus normal. It is hardly necessary to point out that old age constitutes the main predisposition to spontaneous dislocation of the lens, the immediate pathological factor being an atrophy of the fibers of the suspensory ligament: a condition described by Wedl and Bock as "senescence of the zonula."

The writer observed a case of complete bilateral ectopia of the lens. The aphakic portion of the pupil was hyperopic 10 D.; the portion opposite the lens was myopic 13 D. This case and others like it furnish a conclusive argument in favor of Helm-

holtz's view that during accommodation the zonula is relaxed, against the opinion of Tscherning that the act of accommodation is brought about by tension of that membrane. The fact that increase of the refraction is not always observed in luxation of the lens may be due to the circumstance that the fibers of the zonula are not completely torn through—there is subluxation, a comparatively small number of fibers being sufficient to maintain the shape of the lens. Roche (*Rec. d'ophtal.*, Oct., 1909).

**SYMPTOMS; APPEARANCES; VISION.**—Any change in the position of the lens destroys the normal relations between it and the iris, the latter losing its support partially or totally, according to the degree of the displacement, or being unduly pressed forward or backward, or distended, according as the lens is tilted against portions of the posterior surface of the iris, dislocated into the anterior chamber, or fixed in the pupil itself. When the dislocation is incomplete the anterior chamber is deeper at the point vacated by the lens, and the iris of the same region is tremulous on quick movements of the eyes or head. In the slightest degrees of dislocation a slight tremulousness of one portion of the iris may constitute the only physical sign of the lesion, but is an absolute indication that the iris no longer rests on the anterior capsule of the lens. The history of injury and the condition of vision will be necessary to lead to a correct diagnosis.

Increased depth of one portion of the anterior chamber may be accompanied by increased shallowness of another, from tilting forward of some portion of the lens against the iris and ciliary body: a relation which may result in setting up a condition of glaucomatous tension.

By employing focal illumination the edge of the lens can be seen in the pupil,

which, however, usually requires to be dilated for this purpose. The lens itself will appear as a delicate gray compared with the pure black of the aphakic portion of the pupil, and its edge will appear luminous on account of the total reflection which the rays of light entering the marginal portions of the lens from the front undergo at its posterior surface, for at the edge of the lens they strike this posterior surface very obliquely.

With the ophthalmoscope, on the other hand, the edge of the lens appears black, for the same reason, the light coming into this portion of the lens from the fundus being reflected back into the eye.

When there is complete dislocation of the lens there will be an absence of the catoptric lenticular images. The lens itself, when opaque, may be visible through the pupil with the naked eye. As a rule, however, examination with the ophthalmoscope is necessary for its detection. It may be connected with the fundus or freely movable in the fluid vitreous (*cataracta natans*).

There is now more marked and general tremulousness of the whole area of the iris on quick movements of the eyes and head, with an abnormally, but uniformly, deep anterior chamber.

When once seen there is no difficulty in determining the nature of the floating body, on account of its shape and size and the fact that no other condition occurs with which it is possible to confound it.

When the lens is displaced into the anterior chamber its appearance is characteristic, its margin having a golden luster due to total reflection of light, making it look like a large drop of oil in the anterior chamber, which is much deepened, especially at its lower part.



The lens assumes, moreover, a more spherical form than when *in situ*, on account of the loss of the compressing influence of the fibers of the suspensory ligament and choroid, etc. The irritation it sets up often causes a contraction of the pupil behind it.

**CONDITION OF VISION.**—Sight is always impaired to a greater or less extent. In partial dislocation, vision is affected because rupture of the fibers of the suspensory ligament destroys the power of accommodation, and, at the same time, by permitting increase in the convexity of the lens, makes the eye highly myopic. Moreover, the tilting of the lens on its axis induces a variable amount of astigmatism, regular and irregular, lateral displacement having a similar effect.

In higher degrees of displacement, where the edge of the lens lies across the area of the pupil, not only is there a higher degree of visual failure, but there is also diplopia, two blurred images being seen. This is due to the fact that the edge of the lens acts as a prism, and causes the rays of light entering the eye through it to be deviated in the direction of the dislocation, while those entering the aphakic portion of the pupil are unchanged in direction except in so far as they are made to converge and form an indistinct image on the retina.

For the same reason two images of the disk or other parts of the fundus may be seen during ophthalmoscopic examination.

Considered, therefore, with regard to that portion of the pupil still occupied by the lens, the eye is myopic, and the image formed by the light rays passing through it can be cleared to a greater or less extent by concave spherocylindrical lenses. With regard to that part from which the lens is absent, the eye is highly

hypermetropic, and its image can be made clear by the aid of a convex spherical glass, and such a cylinder as is necessary to correct the corneal astigmatism. In a later stage vision may be further impaired by the development of opacities in the lens.

When the lens is completely dislocated into the vitreous chamber, and no complications have arisen, vision resembles that of an eye after cataract extraction, and the condition is exactly similar to that brought about by the operation of reclinacion, or couching.

The patient regains good vision with the aid of strong convex lenses, which have to be adjusted for distance, and also for the near point at which it is desired to read or work.

But in many of these cases complications arise which prevent perfect vision from being attained, or in course of time bring about its impairment in varying degree. Thus, iridocyclitis may arise and destroy vision and even set up sympathetic disease in the fellow-eye. Or glaucomatous tension may occur, with the same result, so far as sight is concerned.

#### **PROGRESS AND RESULTS.**—

Congenital dislocations are always incomplete, and the lens shows no special tendency to become opaque: good evidence that its nutrition is unimpaired. In some cases, however, the displacement increases, and complete dislocation into the vitreous or anterior chamber, or alternately into each, finally occurs. The latter condition is predisposed to by abnormal smallness of the lens: a common characteristic in cases of ectopia, which permits its easy passage through the pupil. When this state of complete luxation has been attained, the lens substance is liable to deteriorate and become opaque. Striking against portions of

the uveal tract the freely movable lens may set up iridocyclitis, and disorganization of the eye and destruction of vision result. Or, as previously stated, secondary glaucoma may become established and finally lead to blindness. Hudson has recently shown that the increase of tension may be due to blocking of the angle of the iris by vitreous protruding through the ruptured zonula and the pupil.

In 2 cases, father and daughter, seen in the practice of the writer, the father, aged 55, had opaque lenses freely floating in the vitreous, and sometimes passing through the pupil into the anterior chamber, with occasional glaucomatous attacks, always relieved by paracentesis. The daughter presented typical examples of ectopia lentis, both lenses being stationary and quite clear. (At a later date this patient's lenses also became freely movable.) Good vision was obtained with convex lenses.

Although there are cases in which a small lens may pass freely through the pupil, as a rule, a lens dislocated into the anterior chamber sets up violent inflammation. The irritation caused by its pressure on the anterior surface of the iris excites contraction of the pupil and iritis, which fix it firmly in position. Or a few white spots indicate the presence of adhesions between the lens and cornea, caused by inflammation of the latter. There is glaucomatous tension and rapid extinction of sight. As a result of the increased tension, ectasia of the anterior part of the sclerotic occurs, and a general enlargement of the eyeball.

Spasm of the sphincter iridis, just referred to, may occur while the lens is in the act of passing through the pupil. There then arise violent inflammatory glaucomatous symptoms.

In a case in which dislocation of the lens into the vitreous occurred as one of the results of the lodgment of a small piece of steel in the eye, the lens was found, after enucleation on account of persistent pain due to absolute glaucoma, to be completely opaque and *black*. The fact that the choroid was apparently entirely devoid of pigment suggests a possible source of the lenticular pigmentation. The foreign body was encysted in fibrous tissue attached to the retina near the equator. The enucleation was performed about twenty-five years after the injury, the eye having been blind for many years.

**TREATMENT.**—When no symptoms other than impairment of vision exist, suitable glasses may be prescribed; but when one eye only is the subject of dislocation, the other being normal and of good visual acuity, the patient will get on better without a correcting glass, depending on the good eye for clear vision. In cases of subluxation, the margin of the lens lying in the pupil, the kind of lens ordered depends upon whether better vision can be obtained by correcting the portion of the pupil containing the lens, the myopic area, or the aphakic, hypermetropic area. This can, of course, only be ascertained by actual experimentation.

Sometimes better vision can be obtained by enlarging the aphakic portion of the pupil by a small **iridectomy**. Other things being equal, this portion is to be preferred for correction on account of the greater size of the retinal images so obtained.

When the dislocation is complete, the lens being in the vitreous, the case is precisely similar from a refraction standpoint to one of aphakia after cataract extraction. Under all conditions two pairs of glasses are required: one for

distance and another for reading or working distance.

But in many cases other symptoms besides disturbances of vision are present at an earlier or later stage in the case. In cases of partial dislocation pressure of the lens against the ciliary margins of the iris and the ciliary body may set up glaucomatous symptoms. In this case, if removal of the lens be not deemed feasible, an **iridectomy** may be made at the point where the lens is in contact with the iris.

Removal of the partially dislocated lens is always difficult, and apt to be complicated with loss of vitreous, on account of the condition of the suspensory ligament, which is either congenitally deficient or damaged by traumatism. In young patients **discission** may be attempted, but its performance can only be effected in some cases by fixing the otherwise movable lens posteriorly with a knife needle introduced through the sclera behind the ciliary zone.

When the lens is dislocated into the anterior chamber, **extraction** is comparatively easy, and, moreover, absolutely necessary. If it is not done, vision is inevitably lost. The lens is fixed in the anterior chamber by the use of miotics or the introduction of Agnew's bident, and the ordinary corneal incision for cataract made. Delivery has to be accomplished by means of the vectis, wire loop, or sharp hook.

When the lens floating in the vitreous causes iridocyclitis or secondary glaucoma, its **removal** is indicated. To do this is a matter of great difficulty. If the case be one in which the lens sometimes passes into the anterior chamber, attempts should be made to bring about this change of position by such movements as have previously effected it. Once in the anterior chamber it should

be fixed there by the use of a miotic or by the introduction of Agnew's bident behind it. If the lens cannot by voluntary movements be made to enter the anterior chamber, it may be brought to the anterior part of the eye by the bident and fixed there. It may then be removed by corneal incision, and its delivery usually requires the use of the vectis or sharp hook. Some vitreous is usually lost, and this is most apt to occur during the removal of the bident, which seems to be the most dangerous part of the operation.

Knapp and Bull maintained that such lenses can be removed, and published reports of cases showing such to be the case, without the use of the bident, and without the introduction of any instrument into the eye, by means of external manipulation only.

When an eye is blind and the seat of absolute glaucoma or of iridocyclitis, due to dislocated lens, the pain so caused is best relieved, and the danger of sympathetic affection of the other eye most effectually avoided, by **enucleation**.

In a case of dislocation of both lenses into the vitreous, of congenital origin, reported by Bickerton in the *Trans. Oph. Soc. U. K.*, 1898, the lens of one eye passed into the anterior chamber, causing reduction of vision to the perception of light and shade. After sixteen days the lens was replaced in the vitreous by a spatula introduced through a corneal incision, with the restoration of perfect vision, the aphakic refraction being corrected.

In a case of a piece of iron embedded in a transparent lens in which the perforation through the anterior capsule has almost closed, an opening should be made in the capsule and the attempt made to extract the foreign body with preservation of the transparency of the lens. As

the cataract caused by this accident is not hard, **linear extraction** is to be preferred up to the age of 40. Elschnig (Münch. med. Woch., April 12, 1910).

### CONGENITAL ANOMALIES.

1. **ECTOPIA LENTIS.** See ANOMALIES OF POSITION.

2. **COLOBOMA LENTIS** is a rare condition due to arrest of development at a late period of embryonic growth. The frequent association of coloboma of the iris and choroid with it suggests its relation to imperfect closure of the fetal cleft. Its immediate cause lies in defective development of the zonula of Zinn. This is developed from adhesions, which form between the sides of the lens and ciliary body during the stage of embryonic life when they are in contact. As the eye enlarges, that portion of the capsule to which adhesions have failed to occur would not be held taut and made to expand like the remainder, and a corresponding depression in the lens would result. Absence of the ciliary body would, of course, be a probable cause of this failure to adhere. Wessely has produced typical coloboma lentis by iridectomy in newborn rabbits. On account of the close relation of the ciliary process and zonula with the posterior surface of the iris in the rabbit, portions of these tissues are removed with the iris.

Heyl has suggested that a defect in the inferior branches of the hyaloid artery, which gives nutrition to the lens while the peripheral fibers are developing, would produce just such a defect.

It is often associated with coloboma of the iris and choroid, and with dislocation and small size of the lens. There is sometimes more or less opacity of the lens.

Tremulousness of the iris has been ob-

served, but more especially in cases in which ectopia also has been present.

The defect usually occurs in the inferior quadrant, but has been seen upward, outward, and down and out.

It resembles in form the chord of an arc, nearly a straight line, but sometimes consists of a complete notch

It may occur in one eye or in both, and is most commonly associated with myopia. Vision is almost always defective, ranging from absolute blindness up to  $V = \frac{1}{4}$ , as a rule. But Bresgin recorded a case in 1874 with  $V = \frac{20}{20}$  and fair accommodation.

Accommodation seems to be usually present in those cases in which vision is good enough to permit of reliable observation of this point. Nystagmus is sometimes present.

A case has been observed in which a projection from the lens margin was associated with a coloboma of the iris.

3. **CONGENITAL SMALLNESS OF THE LENS.**—In these cases the anterior chamber is deeper than normal, and the iris tremulous. The condition can be recognized only after dilatation of the pupil with a mydriatic. An unusually wide space is then seen between the pupillary edge of the iris and the margin of the lens, which stands out as a dark ring against the fundus. Unusual smallness of the lens often accompanies ectopia and coloboma lentis.

4. **APHAKIA.**—Cases of this condition in microphthalmic eyes have been reported, but Lang expresses the opinion that in many the absence of the lens is apparent only, it being really only displaced out of sight.

5. **LENTICONUS.**—This may occur at either the anterior or posterior pole of the lens, the latter being by far the commoner situation. Only two instances of the former are on record, and

there is doubt whether they were congenital or acquired. The condition resembles keratoconus. Anterior lenticonus can easily be recognized by oblique illumination. Jaworski has observed and measured a bilateral anterior lenticonus which subsequently disappeared, in a case of interstitial nephritis and albuminuric retinitis. He regards the case as one of hydrops of the epithelium of the anterior capsule.

Posterior lenticonus requires the ophthalmoscopic mirror for its diagnosis. It gives the appearance of a large oil-drop in the pupil, with a dark, well-defined border. Opacities of the posterior pole of the lens are often associated with it. The refraction is found to be different through the central and peripheral portions of the lens. In one case a remnant of the hyaloid artery was adherent to it. Collins is of the opinion that traction by the artery does not explain this anomaly, which he regards as being due to active development of the lens, causing a bulging of a weak posterior capsule, or the protrusion of lens matter through congenital gaps in the capsule into the vitreous.

Reference may, perhaps, be made here appropriately to the somewhat common cases in which the refraction is found, by estimation with the ophthalmoscope or skiascope, to vary in different parts without any other indication of lenticonus. Sometimes decided differences are found in the upper and lower halves of the pupil. Sometimes the division seems sectional in character.

**6. CONGENITAL CATARACT.**  
(See CATARACT.)

**7. REMAINS OF HYALOID ARTERY AND BRANCHES.**—Punctate opacities, usually situated a little to the inner side of the posterior pole of

the lens, whitish by reflected, dark by transmitted, light, not interfering with vision, discovered incidentally, have been attributed by Ammon de Beck and Mittendorf to incomplete involution of the hyaloid artery.

They are stationary in character, vary in size from a mere point to a poppy-seed, and, although usually well defined, fine lines have been observed radiating from the edge in some cases.

In some cases of persistent hyaloid artery with attachments to the lens, straight vessels have been seen coming from the end of the disk-like attachment to the lens, and disappearing into the ciliary region at the margin of the pupil.

**PARASITES.**—Three kinds of parasite have been described as occurring in the lens: monostoma, distoma, and filaria, the latter occurring in opaque lenses and discovered after removal of the latter on account of the opacity.

F. W. MARLOW,  
Syracuse.

**CUBEB**, *cubeba*, is the dried, unripe fruit of the *Piper cubeba*, a climbing shrub indigenous to Java, Borneo, and Sumatra. The upper portion is globoidal and the base contracted into a rounded stipe. The ovary has a wrinkled appearance and a blackish-gray color, but internally it has a light-brown color, is smooth and oily, and has one seed. Cubeb has an agreeable, aromatic, somewhat camphoraceous odor and taste. It contains a volatile oil, 5 to 15 per cent.; an oleoresin, 6 per cent., which contains *cubebin* and *cubebic acid*; a little *piperin*; a gum, and the malates of magnesium and calcium.

*Oleum cubebæ* is a volatile oil obtained by the distillation of cubeb with water, which deposits, upon standing, rhombic crystals of hydrate of cubebene. The oil is a colorless, pale-green, or yellow liquid. It has an aromatic camphoraceous odor and taste. It contains cubeb camphor, two oils, and a small amount of terpene.

**PREPARATIONS AND DOSE.**—

*Cubeba* (cubeb) is given in the dose of 15 grains (1 Gm.).

*Fluidextractum cubebæ*, N. F. (fluidextract of cubeb) is obtained by maceration and percolation with alcohol, and then evaporation. Dose, 15 minims (1 c.c.).

*Oleoresina cubebæ* (oleoresin of cubeb) is obtained by percolation with alcohol, distillation, and then evaporation of the alcohol. Upon standing it deposits a waxy, crystalline material, which should be rejected. Dose,  $7\frac{1}{2}$  grains (0.5 Gm.).

*Trochisci cubebæ* (troches of cubeb), contain 2 parts oleoresin of cubeb, 1 part oil of sassafras, 25 parts extract of glycyrrhiza, 12 Gm. (3 drams) acacia, and syrup of Tolu enough to make 100 troches.

*Oleum cubebæ* (oil of cubeb) is given in the dose of 8 minims (0.5 c.c.).

**PHYSIOLOGICAL ACTION.**—When applied to the skin cubeb acts as an irritant and rubefacient.

Internally, small doses of cubeb improve digestion and increase the appetite, while large doses cause gastric and sometimes intestinal irritation, with nausea, vomiting, abdominal pain, and sometimes diarrhea. The chief action of cubeb is upon the mucous membrane of the genito-urinary tract, acting as a stimulant and disinfectant. By stimulating the functional activity of the kidney it is also a diuretic. Albumin, or blood, or both may be found in the urine after large doses of the drug have been taken, owing to the severe renal irritation produced. Sometimes a papular or erythematous rash is caused, which disappears a few days after the administration of the drug is stopped, and is followed by desquamation. Cubeb is said to increase the force and frequency of the heart. It is eliminated by the kidneys, lungs, and skin.

**THERAPEUTICS.**—Cubeb is used in the treatment of genitourinary diseases, particularly **gonorrhea**, being considered of most value in the acute stage, and is often combined with copaiba in this condition. It is also used in **chronic cystitis**, and sometimes relieves **functional irritability of the bladder**, and checks **nocturnal incontinence of urine**. The oil has been used, both by injection and by mouth, in the treatment of **leucorrhea**. In certain

diseases of the respiratory tract this drug is of value. In **acute rhinitis** the powder may be used by snuffing up the nostril, and cubeb cigarettes often relieve an attack of **asthma** or **hay fever**. It is also of considerable value in **subacute** and **chronic bronchitis**, while the troches are used by public speakers and vocalists where **pharyngitis** or **laryngitis** is present to any degree. H.

**CUPPING** is a method of relieving inflammation by drawing the blood away from the inflamed area. *Dry cupping* is the term used when the blood is only drawn to the surface and acts as a counter-irritant; in *wet cupping* the blood is drawn from the body, acting as a counterirritant and depletant. The skin should be washed and dried before applying the cup.

In **dry cupping** a small tumbler or glass may be used the edge of which has been oiled. A small piece of blotting paper soaked in methylated spirit is placed in the glass and ignited; the glass is inverted and firmly placed over the part to be cupped. A partial vacuum is formed in the glass, and the soft tissues are drawn up into the glass and become deeply congested by the dilated blood-vessels. When wishing to remove the glass, the finger is pressed under its edge and the air rushes in.

**Wet cupping** is done in the same way except that the skin is scarified just before the cup is applied, and as much blood may be withdrawn as is desired. This method should not be applied on exposed surfaces, as the wounds made leave a permanent mark, and should not be used in feeble persons who cannot stand loss of blood.

Cupping is often efficient in inflammatory lung and renal diseases, relieving the congestion and stasis in these organs. They should be applied over the base of the organ. It has also been used in **intermittent fever** during the first stage, several cups being applied along the spine. Cups should not be used in acute pleurisy or peritonitis, for fear of injury to the parietal serous membrane.

The writer attests the value of blister cupping in **pulmonary edema**. The usual drawbacks of cantharidin

blisters may be avoided, he found, by using an ordinary tumbler, with a lighted, crushed up piece of newspaper inside, applied to the skin in the dorsolumbar region. The tumbler is pressed firmly into the skin and left there for 1½ or 2 hours. Multiple blisters form under it, and they continue to secrete for about a week. They are used for visceral congestions, renal and sciatic pains, etc. Aubert (Lyon méd., cxxiv, 3, 1915). H.

**CUSO**, sometimes called brayera and kouso, is the dried female flower of *Hagenia abyssinica*, a tree of Abyssinia. It occurs as compressed bundles or rolls having a reddish-brown color, slight odor, and a bitter taste. The larger stems should be rejected. Cusso contains gum, tannic acid, and two resins; also *koussin*, a volatile oil, which is the neutral active principle of the drug, occurring as yellow, tasteless crystals, insoluble in water, but soluble in alcohol, ether, chloroform and benzol.

**PREPARATIONS AND DOSE.**—Cusso, or kouso, is given in the dose of 4 fluidrams (16 Gm.). It is not official.

**PHYSIOLOGICAL ACTION.**—Kouso is an anthelmintic and gastrointestinal irritant, large doses causing nausea, vomiting, diarrhea, and sometimes prostration, collapse, and irregularity of the pulse. It should not be used during pregnancy.

**THERAPEUTICS.**—Kouso is used exclusively in the treatment of **tapeworm** (*Tania solium*), and should be taken in the morning on an empty stomach. The efficiency of the drug depends upon the freshness of the flowers. H.

**CUTAL.** See ALUMINIUM.

**CYSTITIS. — DEFINITION.** — Inflammation of the urinary bladder, involving one or more of its four coats: mucous, submucous, muscular, and serous, and, according to modern pathology, it is invariably due to germ infection.

**VARIETIES.**—Cystitis has been divided into a large number of varieties, the subdivisions being based upon the

many etiological and pathological features of the disease. A further classification of this disease into the acute, the subacute, and the chronic is dependent upon the intensity of the symptoms and the length of time of their existence and is utilized in this article. The following micro-organisms, the cause of cystitis, mentioned in the order of their relative frequency of occurrence, are the *Bacterium coli communis*, streptococcus, *Bacillus tuberculosis*, gonococcus, and *Bacillus typhosus*. These bacteria gain entrance to the bladder in one or more of four ways, to wit: through the urethra, the blood or lymph channels, the kidneys, and the wall of the bladder.

These germs exert their injurious action upon the bladder either directly or through their ptomaines. The inflammation thus produced is increased by the ammoniacal fermentation of the urine which the bacteria bring about. This fermentation is due to the decomposing action of microbes upon urea, with the resulting formation of ammonium carbonate. This fermentation is the result, and not the cause, of cystitis.

**SYMPTOMS.**—In **acute cystitis** the commencement differs somewhat according to the determining cause. When traumatic, it may be ushered in with rigors or marked chill, succeeded by burning pain in the bladder and glans penis, etc. In other instances, and when from other causes, it is announced by a feeling of uneasiness, which is located in the perineum. There is increased frequency of urination and spasmodic pain during micturition and more or less fever. Usually the fever is absent, but in the severe forms there is moderate fever, and sometimes, in the pseudo-membranous variety, quite high fever.

Case of membranous cystitis in a colored woman with no evidence of gonorrhea. Acute cystitis occurred with sudden onset. The symptoms for the first week were very severe. Three weeks later the urethra became blocked by a sloughing mass, which on removal proved to be an entire cast of the bladder, consisting of the mucosa and a portion of the muscularis. Symptoms from this time began to subside, and two months later the patient was entirely well. This case had no assignable cause. The uterus was in normal position, there were no neoplasms blocking the pelvis, nor was the patient pregnant. No strong chemical solution had been used in the bladder. Norris (*Amer. Medicine*, March 31, 1906).

Usually the temperature in cases of fever ranges from 100° to 102° F., though it may be higher. These constitute the ordinary symptoms. Pressure over the region of the bladder is intolerable. The urine may be blood-tinged throughout the attack, but more usually is replaced soon by pus, and becomes ammoniacal. Acute retention is common.

Three cases of incomplete retention of urine due to chronic cystitis. In 2 cases the infection was with gonococci, in the third probably with the colon bacilli. In chronic cystitis the retention is due to the pathological changes in the muscles of the bladder. In the first stage of the disease the muscle is hypertrophied by overwork. In the second stage a sclerous hypertrophy follows, and in the third stage an atrophy. Some of the muscle-tissue remains, but is not well co-ordinated. The fatty tissue is infiltrated among the muscle-fibers and disturbs the retraction of the bladder, and this leads to retention. When fluid is injected into the bladder, the desire to urinate becomes intense, while the contractility of the bladder is little accentuated. The urethral sphincter is not involved in the process, so that incontinence does not

usually result. There may be incontinence, due possibly to an increased sensibility or to a participation of the urethral sphincter, which plays an important part in the act of micturition. Acute retention comes on sometimes in chronic cystitis and is to be explained by attacks of acute cystitis, which produce an inhibitory action upon the bladder muscle. Cealic and Strominger (*Ann. d. mal. d. org. gén.-urin.*, vol. ii, p. 1787, 1909).

If complete retention ensues, the bladder gradually becomes more and more distended and can be felt as a rounded tumor, giving a dull sound on percussion, rising higher and higher above the pubes. The tenesmus vesicæ, or the feeling that the patient has not emptied the bladder after the viscus has been emptied, may occasionally be communicated to the rectum, and, in point of fact, all of the pelvic organs may participate in the painful and distressing sensation.

The frequent desire to pass water varies in intensity. It may be every few moments or almost incessant, several times an hour or once in a couple of hours.

The constitutional disturbance, when the disease is of grave form, is very marked, as indicated by a frequent pulse, thirst, headache, and nausea, with great restlessness and mental anxiety. When cystitis progresses toward a fatal termination, portions of the wall of the bladder may suppurate or even slough, and may be discharged in stringy fragments; the urine emits a vile odor, from the products of its own decomposition and the gases resulting from the dead mucous and submucous tissue which it contains; the patient is harassed with hic-cough; the pulse becomes very small and frequent, the tongue dry and hard, streaked with a dark coat; the strength



rapidly fails; the secretion of the kidneys diminishes or is entirely suspended; the countenance becomes sunken and cadaverous, the extremities cold, the surface moistened with perspiration, from which emanates the odor of urine, and the patient at last passes into a state of profound stupor, from which he never awakens.

In **chronic cystitis** the symptoms are mainly those of the acute variety, but in a milder degree. Only slight fever is present, but the combination of pain and other distress rapidly undermines the general health.

The urine is turbid, alkaline, and contains much mucus and pus, which forms a tenacious clot at the bottom of the retaining vessel. While the urine is usually alkaline, it occasionally is faintly acid when first passed, but, if so, promptly becomes alkaline upon standing, due to the formation of ammonium carbonate out of the normal urea, probably due to the action of bacteria.

The greater alkalinity thus resulting reacts upon the pus and converts it into a glairy matter similar to mucus, thus further increasing the difficulties of urination.

"Cystitis senilis feminarum" is a condition of the bladder peculiar to women who have long passed the stage of menopause. The ages of the patients suffering with this condition are nearer 70 than 50. In 1 out of 50 cases in the author's experience the bladder picture as described occurred in a patient of 38 years. But this patient had had 1 child and had not menstruated for 13 years. Clinically there is undue frequency of urination with tenesmus and burning. Loss of sleep and suffering attend the acute stage which may last from several weeks to months. Then follows a stage of comparative comfort. Recurrences are common. The cystoscopic pic-

ture is characteristic. Vesiculo-papular elevations, usually discrete on a deeply injected mucosa, more or less sharply defined from the healthy mucosa are to be seen at the height of the attack. The vesicles may become purulent and break. In the interval stage there is a scattered number of flat pigmented and ecchymotic patches. F. R. Charlton (Surg., Gynec. and Obstet., Oct., 1916).

**DIAGNOSIS.**—This is usually easy. Yet there sometimes occur mild forms which it is difficult to differentiate from mild degrees of interstitial nephritis, while it not very rarely happens that these two conditions are associated. In contracted kidney there are sometimes many leucocytes also. The presence of hyaline casts, even when scanty, points to nephritis, while hypertrophy of the left ventricle and increased arterial tension settle the question. Still more emphatic is the diagnosis if there be retinitis albuminurica (Tyson). According to the same authority, the question whether there is pyelitis, separate or associated with cystitis, is still more difficult to determine. Catheterism of the ureter by the method of Howard A. Kelly, if a possible procedure in a given case, would, of course, clear up all doubt. Tyson places most reliance on the symptom of tenderness in the region of the kidney.

Many patients suffering from chronic cystitis fail to respond to treatment. This is due to inaccurate diagnosis. The latter requires, in most instances, three examinations to determine whether or not diseases of adjacent viscera are causing or apt to cause the urinary infection: 1. Examination of the urine, including a passed specimen and a catheterized specimen taken with all aseptic precautions. In the female, after sterilization of the parts, it is advisable to

pack sterile gauze around the urethral orifice before inserting the catheter. The bacteriologic examination should be done as soon as possible. 2. Rectal examination of the male to exclude diseases of the prostate, seminal vesicles, fissure, fistula, and hemorrhoids, and both rectal and vaginal examinations of the female to exclude uterine enlargements and displacements, adnexal disease, and cystocele. 3. Abdominal examination for bladder distention or tenderness, and pathologic processes in the appendix or kidney. An X-ray examination of the whole genito-urinary tract should be made and followed by a cystoscopy and pyelography. Dobson (Brit. Med. Jour., ii, 305, 1921).

Usually the symptoms of the diseases under discussion leave scarcely any room for doubt; the sense of uneasiness in the neighborhood of the bladder, the frequent desire to empty that organ, and the thick, purulent urine, taken in conjunction with microscopic examinations, will render the diagnosis certain. It is very important to ascertain whether the cystitis is idiopathic or the result of disease of the urethra, prostate, etc., and especially whether a foreign body, such as a calculus or tumor, is present in the bladder. In these cases of foreign bodies cystoscopy, in the hands of the expert, is of great value from a diagnostic standpoint. It is also important to differentiate spasm of the bladder, which is also attended by pain and frequent micturition; but the quality and the daily quantity of the urine passed remain normal.

In polyuria also the urine is voided frequently, but without any pain or purulent sediment (Lebert).

One in every 5 of the writer's gynecological patients has complained of disturbances in urination, and 1 in every 8 has exhibited chronic cystitis of the neck of the bladder. In two-

thirds of all the cases with urinary disturbances, cystitis of the neck was evident. The cystitis may be attributed to infection, to venous congestion, or to hyperplasia. Knorr (Zeit. f. Geb. u. Gynäk., Bd. Iv, Ols-hausen Festsch., 1905).

The question of whether the pus present comes from the bladder, the urethra and prostate, or the kidney may be positively solved by having the patient urinate in two glasses. If pus is present only in the glass first used, then it is certain that it comes from the urethra or its neighboring glands. When pus is present in the second vessel, its source may be either the bladder or the kidneys, or both. The differential diagnosis between a cystitis and a pyelitis is not so readily determined.

Pus in the urine is usually microscopic when coming from an inflammation of the bladder. The *three-glass test* is a valuable aid in locating the source of the pus. If the first portion of the urine contains pus, while the second and third contain none, the pus comes from the urethra. If the first portion contains a great deal of pus, the second portion less, and the third none, the inflammation has not extended beyond the vesical orifice. If the first glass contains pus, the second none, and the third has pus in it, the source is the prostatic urethra. But if all three portions contain pus, there is a cystitis. The cystitis may be associated with a pyelitis or suppurating kidney, which must be determined. E. O. Smith (Lancet-Clinic, July 2, 1910).

Catheterization of the ureters, cystoscopy, and in some cases the use of the X-rays are the most trustworthy means of clearing up the doubts.

Two cases of mysterious intermittent fever in children of 4 and 5. On inquiry it was ascertained that the children had complained of pain at micturition, and this gave the clue for discovery of the cystitis by mi-

roscopic examination of the urine. The urine should be examined as a routine measure in all cases of intermittent fever and chills of unknown origin, especially those which suggest intestinal or malarial affections. R. Petrucci (Policlinico, April 28, 1912).

All known means and methods should be employed in forming our diagnosis, including the use of the urethroscope, cystourethroscope, or the cystoscope and the radiograph. A diagnosis of cystitis should not be made from the presence of frequent urination, pain, and pyuria, especially if the case is of a chronic character; when vesical irrigations do not cure the trouble, it should not occasion surprise, and, finally, if there is reason to believe that cystitis is present, the underlying cause should be ascertained before beginning treatment. Clark (Med. Record, March 30, 1912).

**ETIOLOGY.**—The causes are predisposing and exciting. Men are more liable than women to vesical catarrh. Among the predisposing factors traumatism is a frequent cause; injuries, such as blows and pelvic fractures, more particularly of the pubic bone, though both are rather rare conditions. Operations of lithotomy, lithotritry, catheterism, injections; pressure, as in prolonged and instrumental labors, in which class of cases gangrene of the coat of the viscus has been known to ensue, followed by a large vesicovaginal fistula. Abdominal, gynecological, and rectal operations are prominent causes of cystitis owing to the opportunity they afford for infection of the bladder.

The writer found but 380 cases of cystitis among 10,000 gynecological cases and regards coitus as a cause. Only 1.5 per cent. of the cases occurred in virgins, 2.5 per cent. in widows, but over 5 per cent. in married women. Of the 3 cases in little girls 2 were due to gonorrhea following attempted coitus; 4 cases

resulted from the use of catheters, and in 22 cystitis was referred to syphilis, typhoid, tuberculosis, and lithiasis. In only 45 was there no accompanying disease of the urethra and genital organs. Menstruation, the climacteric, and early pregnancy seemed to have no influence upon the condition, though menstruation apparently caused an exacerbation of existing cystitis. Vedeler (Norsk Mag. f. Laeger.; Zentralbl. f. Gynäk., Nu. 42, 1902).

Postoperative cystitis occurs more frequently after abdominal operations in which there is a combination of traumatism and bacterial infection, as in abdominal hysterectomy in which the bladder is released from its ordinary attachments, its resisting power diminishing. The infecting germs may be already in or upon the tissues traversed by the catheter or they may be conveyed from without. Johnson (Amer. Jour. of Obstet., June, 1910).

The frequency of cystitis after operations on the rectum is noticeable. It occurs even when the patients have not been catheterized. As it is usually of a hemorrhagic character, it is probably the result of thrombosis in the bladder veins. In 153 operations on the rectum, 61.4 per cent. of the patients required catheterization and cystitis developed in 50 per cent. of these. It came on between the third and sixth day as a rule, and in about half the cases of this hemorrhagic cystitis the trouble began with severe hemorrhage. Postoperative cystitis developed in only 12 of 46 patients requiring catheterization in a series of 239 laparotomies in the last three years, and in none of these was the cystitis hemorrhagic. Hadda (Berl. klin. Woch., Aug. 22, 1910).

Cystitis following surgical operations is not always due to catheterization. For its production it is necessary to have a bacterial infection plus retention, trauma, and congestion. The colon bacillus is the organism most frequently found in

cystitis following surgical operations. Such operations also require the most rigid asepsis in their after-care, should catheterization be required. The use of a solution of 2 per cent. boric acid in sterile glycerin injected through the urethra, into the bladder, has proved itself of sufficient value to warrant its routine employment in all cases of postoperative urinary retention before resorting to catheterization. Jacobson and Keller (Jour. Amer. Med. Assoc., Dec. 16, 1911).

Bacteria in the bladder do not cause infantile cystitis without some predisposing factor such as a debilitated state of the bladder walls from distention by retention of urine, circulatory irregularity, the presence of a calculus, or foreign body. Cantharides plasters should never be used in infancy as the tender skin absorbs the cantharidin which in the process of elimination inflames the bladder. Gastro-enteritis is almost always accompanied by a cystitis, as is also vulvovaginitis and the urethritis produced by masturbation with foreign bodies in the urethra. J. Vecina y Lopez (Archivos de med. interna, Sept., 1917).

Mechanical irritation of foreign substances in the bladder, such as calculi; the poisonous effect of certain drugs, as the chemical action of cantharides and some of the mineral poisons; the action of the urine itself, retained and decomposed, as in stricture and in prostatic enlargement; inflammations of neighboring parts, as the kidneys, prostate, rectum, urethra, and, when so developed, it is in consequence of a pre-existing gonorrhea, a prostatitis, or the presence of a stricture—urethral or rectal—etc.; acute cystitis sometimes develops secondarily in the course of the infectious diseases.

A large number of cases of cystitis due to the influenza bacillus are on record. The writer's patient was a woman of 35 with acute catarrhal gastroenteritis and the influenza ba-

cillus in the blood. As the symptoms of this were subsiding, signs of urethrocystitis developed and the temperature ran up again. It subsided the fourth day with a crisis and the symptoms on the part of the urethra and bladder had all disappeared by the end of the week. Comby has reported 3 cases of painful, rebellious, and hemorrhagic cystitis also of influenzal origin. G. Ghedini (Gaz. degli Ospedali, Aug. 21, 1910).

The organism isolated by the writer from cystitis urine is a member of the colon subgroup. It fermented dextrose, lactose, dulcitol, mannitol, maltose, raffinose, adonitol and inulin with the production of acid and gas without any delay, whereas it did not ferment saccharose. The gas production through this organism was the strongest in mannitol and maltose, and then in dulcitol, lactose, dextrose and adonitol, while in raffinose and inulin it was the weakest. The acidity produced was most marked in mannitol, maltose, dulcitol, and lactose, and then in dextrose and adonitol, while in raffinose and inulin it was only feeble. This organism proved to be pathogenic and pyogenic to animals. The serum of the patient in question showed a strong agglutinating power to this organism. Niwa (Jour. Med. Research, Mar., 1919).

J. W. White and Edward Martin hold, in common with the leading genitourinary specialists of today, that all cases of cystitis are undoubtedly due to the presence of pathogenic organisms, which are the exciting causes of this malady.

The writer, in a number of cases, tested the action of the patient's blood-serum upon the specific bacteria found in the disease. In a case of cystitis of many years' standing caused by the *Bacillus coli communis*, a pure culture of the bacillus showed well-marked clumps in ten minutes after the blood-serum, diluted ten times, had been added to it. A case of cystitis and pyelitis due to the *B. proteus vulgaris* gave a similar re-

action in the same time with a pure culture of the *B. proteus vulgaris*, but another of four years' duration failed to do so even after sixty minutes. Another case of acute cystitis, supposed to be due to the *B. typhosus*, gave a positive reaction in dilutions of 1:80, and, so far as could be ascertained, the patient had never suffered from typhoid fever. Brown (Boston Med. and Surg. Jour., Nov. 8, 1900).

Series of 40 cases of cystitis following gynecological operations examined bacteriologically on the first day of their inception. Streptococci were found in 6 specimens of urine, staphylococci in 34, and in 10 colon bacilli in addition to the two former. The latter were never found in any urine before operation, but in cystitis persisted as late as the third or fourth week. Postoperative cystitis is due to primary staphylococcus or streptococcus infection, with subsequent infection with the colon bacillus. Repeated examinations of the urethra, vestibular region and vulva, convinced the writer that the infection always comes from without, and usually through catheterization. Baisch (Beiträge z. Geburtsh. u. Gynäk., Bd. viii, H. 2, 1905).

Series of 80 cases of pyelocystitis in infancy derived from a large foundling hospital. Many of the infants suffered from nutritional disorders, while infections, particularly influenza, were very common. The series included 58 females and 22 males, tending to show that the disease is much more common among males than previously believed. The youngest child was 11 days, the oldest 22 months. The colon bacillus was demonstrated in a number in this series. The proteus bacillus was found twice, the *B. lactis aërogenes* once. During the year ending February 1, 1910, there were 22 cases of pyelocystitis; one-half of these occurred in the months of November, December, and January, during a severe epidemic of gripe; 59 of the cases were directly preceded by

either some infection or an acute nutritional disorder, while only 7 occurred under observation which were not preceded by a previous serious disorder. The 14 remaining patients entered with this condition; 21 cases were preceded by some infection of the respiratory apparatus, of which 7 were influenza and 2 diphtheria; 12 others by otitis media, 7 by alimentary intoxication, 6 by septic conditions, 5 by enteritis follicularis, 4 by stomatitis, 2 by active syphilis with profuse eruption, and 1 each by tuberculosis and vaginitis. Out of 20 necropsies the kidney pelvises and bladder both showed pathological changes in 15 instances; 3 times the pelvises were alone involved, once the bladder alone, and in 1 instance there were no pathological findings in the urinary apparatus, although the child had had pyuria six weeks previous to death. E. B. Friedenwald (Archives of Pediatrics, Nov., 1910).

In male infants infection of the bladder may take place in three ways: (1) ascending infection through the urethra; (2) through blood-stream from kidney; (3) passage of bacteria directly into bladder through intestine. In females infection usually takes place through the urethra. In males, on the other hand, infection does not take place through the urethra, but either by means of the blood-stream from the kidney, and then to the bladder, or directly into the bladder from the intestine. According to Escherich, infection from the intestine to the bladder is the more common means of infection. Infection through the intestine always means an enteritis before the bladder becomes involved. The authors report 4 cases of cystitis with complete autopsies. In 3 cases infection took place through the intestine. The organisms which caused the cystitis were *Bacillus bifidus communis* and a paracolibacillus in 1 case; paracolibacillus in the second; *Bacillus proteus* in the third. In these 3 cases a severe enteritis preceded the cys-

titis, and there is no doubt in the authors' minds that infection took place from the intestines. The fourth case was one of tuberculosis. Here infection is supposed to have taken place from the lungs by means of the blood-stream. Rach and von Reuss (Jahrb. f. Kinderheilk., Dec., 1911).

Cystopyelitis of newly married women, which supervenes promptly upon defloration, is always unilateral, and is caused by *Bacillus coli*. Wildbolz proposed to term the condition defloration pyelitis. A non-gonorrheal cystitis in newly married women has long been known. A coli infection of the female bladder occurs under various conditions. The urethral orifice is directly exposed to injury by the penis. Coitus becomes painful and the patients even shrink from the digital exploration. Attempts at coitus doubtless are responsible for the accidental introduction of the bacilli in the urethra. Sippel (Deut. med. Woch., June 6-13, 1912).

The cause of cystitis which is often fatal in cases of urinary retention due to injuries of the spinal column, is almost invariably attributable to catheterization. This is shown by an analysis of all the records of a 1500 bed general hospital covering a period of 20 years, during which time there was no case of spontaneous rupture of the bladder from paralytic overdistention. Cases have been encountered in which there was distention up to the umbilicus for months and when recovery finally took place both bladder and kidneys regained their normal functions with great rapidity. F. A. Besley (Jour. Amer. Med. Assoc., Aug. 25, 1917).

While all the pyogenic bacteria are capable of producing inflammations of the bladder, and most of the known forms of bacteria have been isolated by sundry investigators, those of the colon group are the most frequent cause of cystitis, both acute and chronic. Bacteriological studies have further shown the old idea to be no longer tenable that an

acid cystitis is usually due to the tubercle bacillus, for as a matter of fact, the urine in the vast majority of cases in simple cystitis is acid. The colon bacillus, the staphylococcus, different varieties of the streptococcus, the gonococcus, and many other organisms are usually associated with an acid cystitis, while organisms belonging to the proteus group usually produce an alkaline cystitis, with the well-known ammoniacal, ropy, mucoid condition of the urine. There is a peculiar specificity displayed by different bacteria for different parts of the urinary tract. Thus, the primary focus of tuberculosis in the urinary tract is well known to be practically always in the kidney, vesical tuberculosis being secondary to the infection above, when it occurs. The gonococcus has a special predilection for the mucosa of the urethra; the only portion of the bladder commonly involved is the trigone, diffuse gonorrheal cystitis being extremely rare, while proven cases of gonorrheal infection of the kidney are rarer still. The typhoid bacillus, on the other hand, attacks principally the kidney, and usually produces a lesion of mild degree, resulting in nothing more than a bacilluria. The colon bacillus, staphylococcus, streptococcus, pyocyaneus, and some other organisms attack the kidney, bladder, and posterior urethra apparently with equal facility. With the possible exception of the tubercle bacillus, there is nothing characteristic in the lesions produced by these various bacteria, and it is impossible from the symptoms or pathology of a vesical lesion to determine the variety of invading organism. Geraghty (Surg., Gynec. and Obstet., xxiv, 655, 1917).

**PATHOLOGY.**—The changes which are produced by cystitis consist in increased vascularity of the mucous membrane; its light-red color being exchanged for one of a dark-crimson hue throughout, deepening to purple or even

black about the neck of the bladder, or the mucous membrane may be ecchymosed, and in places necrotic, and the muscular layer may be exposed. Hemorrhages may occur from bursting veins or separating sloughs, or perforation may occur into the surrounding tissues or into the peritoneal cavity. Peritonitis may arise without actual perforation.

In the more chronic cases the epithelium desquamates very rapidly; mucus at first and then pus are poured out in large quantities. The urine soon becomes alkaline, and is putrescent. Blood is frequently present. Decomposition precipitates the salts of the urine, and calculi are formed in the bladder, or a calcareous deposit occurs upon the walls of that viscus. When the disease has been of long duration the muscular wall becomes either hypertrophied and contracted, or its fasciculi become irregularly stretched apart while the mucous membrane sinks into the intervals, giving rise to the condition known as sacculated, or ribbed, bladder. These depressions or sacs may become large and retain decomposed urine, act as receptacles for calculi, or perforate and give rise to peritonitis or perivesical abscess. The ureters and kidneys soon become involved, and add materially to the serious nature of the case. Cysts may also occur, giving rise to the form known as cystitis cystica.

**PROGNOSIS.**—The prognosis will depend on the ability of the surgeon to remove the cause and on the duration of the disease. Ordinary acute cystitis, when uncomplicated, is not attended by any great danger. Protracted cases of acute vesical catarrh do occur and may run a very chronic course. The chronic form is to be regarded as troublesome and very intractable, and rather dangerous to life.

In young and middle-aged patients, and in those of good constitution, the prognosis is more hopeful and the treatment is more effectual than in those who are advanced in years or enfeebled by disease.

**TREATMENT.**—Our first efforts should be directed to a removal of the cause. If a suppurating kidney is the source of the trouble the renal disease must be mastered; **strictures** must be **dilated** and **stones, tumors, and foreign bodies** be **removed**, etc., before a cure can be obtained. When residual urine is present, or paralysis of the muscular coats of the bladder exists, daily **catheterization** is essential prior to relief being effected. As infection from specific micro-organisms is the cause of the malady, we must be on the alert to remove those present and prevent further contamination. Careful **aseptic preparation** should precede all instrumentation, and not only should the instruments be sterilized, but the genitals of the patient and the hands of the operator should be cleansed, as is done in preparing for an operation of more note.

Chief points in the prophylaxis of postoperative cystitis: 1. Try to avoid retention by the use of one or several of the following methods: **filling the bladder with sterile water** at the conclusion of the operation; injecting **boroglycerin** solution into the full bladder; having the patient sit up out of bed as early as the nature of the operation will allow. 2. In the operation, handle the bladder carefully and cover its denuded surface as well as possible before the close. 3. Prevent the introduction of germs from the urethra as far as possible, by using a double catheter such as devised by Rosenstein. 4. Internally, you may give **urotropin, helmitol**, etc. 5. Above all, wherever catheterization has to be continued for some

time, irrigate the bladder each time with 1 to 2 pints ( $\frac{1}{2}$  to 1 liter) of **boric acid** solution and continue such irrigations with each catheterization, not merely until the first spontaneous urination, but until there is no longer any residual urine. Taussig (Surg., Gynec. and Obstet., Feb., 1906).

In **acute cystitis** the patient should be in bed. The **diet** should be light and unstimulating: milk, broths, eggs, etc. Stimulants are to be avoided.

The bowels should be regulated by the administration of a **saline**. In point of fact, all such cases are better for the use of some drug, as the **citrate of magnesia**, **Epsom salt**, **Apenta** or **Hunyadi water**, etc., employed to the point of free purgation. James Tyson claims that **leeches** should be applied to the perineum more frequently than they are. **Hot applications** exert a most beneficial effect upon these cases, relieving pain and strangury. They may be used in baths—sitz or otherwise; cloths wrung out of water as hot as the patient can stand, applied to the perineum or the suprapubic region, or, better still, the thermo bags or bottles, of which a variety of forms may be obtained in any large city.

Acute pyelocystitis is being overlooked in infancy because of the neglect of a routine microscopical urinary examination in all cases. That acute pyelitis is always an ascending infection with the colon bacilli from the soiling of the vulva, is losing ground. The blood-stream infection route is the more probable. Acute pyelitis is probably never primary. The disease, as a rule, responds promptly to the alkaline treatment, especially **potassium citrate** or **guaiacol**, through rendering the urine alkaline. Urotropine and vaccines are most disappointing. C. A. Sellers (Jour. Ind. State Med. Assoc., Mar. 15, 1918).

Frequent micturition may be relieved when the cystitis is not due to a growth, foreign body, tuberculosis, or malignant trouble by the tincture of **belladonna**, especially when it is given with the bromides or other agents which tend to reduce the irritability of the cystic sensory nerve-endings and that of the spinal centers. The following prescription is useful:

R *Potassii acetatis* ..... ℥ss (15 Gm.).  
*Potassii bromidi*,  
*Sodii bromidi* ..... āā 3ij (8 Gm.).  
*Tinct. belladonnae fol.* f3ij (8 c.c.).  
*Syr. limonis* ..... f3j (30 c.c.).  
*Alcoholis*,  
*Glycerini* ..... āā f3iij (12 c.c.).  
*Aqua menth. pip.*,  
q. s. ad ..... f3iv (120 c.c.).

M. Sig.: Teaspoonful in water every two hours.

If the urine is acid it should be rendered neutral by **alkaline drinks**. For this purpose H. C. Bloom recommends **Vichy water** containing much soda. In most cases the urine is alkaline, though not as frequently in the acute cases as in those that are chronic. The best remedy for neutralizing an alkaline urine is **benzoic acid**, either administered in solution well diluted with water or in capsules containing 5 grains (0.3 Gm.) of the drug, administering every three hours until the desired result is obtained. Considerable water should be taken after each capsule. When there is much ammoniacal decomposition, **salol**, in capsules of 5 grains (0.3 Gm.) each, given every two hours until the urine is rendered acid, is a valuable remedy. **Boric acid**, in 10- or 20-grain (0.6 to 1.3 Gm.) doses, is often efficacious. A weak **nitrate of silver** solution is recommended by some surgeons, but, as a general rule, local treatment is contraindicated in acute



cystitis; an exception exists, however, in cases due to gonorrhea.

A most excellent remedy for gonorrheal cystitis in women is a 1:15 suspension of **ichthylol** in glycerin. A urethroscopic tube is introduced through the urethra, and an application made first to the trigone by means of an applicator dipped in the ichthylol mixture. The endoscopic tube is then withdrawn until the applicator projects about an inch beyond the lumen of the tube within the urethra. The applicator and tube are now slowly withdrawn, maintaining the same relative position. In this way the walls of the urethra are kept on the stretch, and all folds smoothed out, so that the applicator following thoroughly swabs the entire canal. This treatment is given every other day, until stained specimens no longer show gonococci. Lockwood (Southern Cal. Pract., vol. xviii, No. 4, 1903).

When occurring in the course of gonorrhea cystitis appears usually in the first weeks of the acute stage, and is often provoked by the use of injections. It is best treated by the daily instillation of 20 to 40 minims (1.25 to 2.5 c.c.) of a 2 to 5 per cent. solution of **nitrate of silver** into the empty bladder through a Guyon syringe. Cystitis associated with prostatic hypertrophy and a contracted and irritable bladder is also best treated in this way, but if the bladder is readily dilatable vesical lavage should be carried out daily, using nitrate of silver solution, 1:1000. If the nitrate of silver causes much pain it may be replaced by **protargol**. Tuberculous cystitis requires especial attention to the general health of the patient. Locally, lavages are contraindicated, instillations alone being permissible. Nitrate of silver here usually aggravates the symptoms; **mercuric sublimate** 1:10,000, or **guaiacol** in oil 1:20, is much to be preferred. E. Michon (Archives gén. de méd., vol. i, p. 402, 1905).

Severe case in a young woman, 26 weeks pregnant, in which the turbid

urine showed many amebæ, mostly spherical, together with some cysts. **Emetine hydrochloride** was given hypodermically in daily doses of 1 to 3 grains (0.06 to 0.2 Gm.). At first improvement was but slight. Later, the bladder was repeatedly washed out with **boric acid** solution and  $\frac{1}{2}$  grain (0.03 Gm.) of emetine in  $\frac{1}{2}$  ounce (15 c.c.) of sterile water left in the bladder. Uninterrupted improvement followed. E. J. Wright (Jour. Trop. Med. and Hyg., July 2, 1917).

In such cases where the inflammation is too acute to tolerate irrigations, instillations of **nitrate of silver** are of great value. They should be given with the Ultzmann or the Otis syringe, beginning with a strength of a grain (0.06 Gm.) to the ounce (30 c.c.) and increasing the strength to 10 grains (0.6 Gm.) if necessary. From 5 to 20 drops (0.3 to 1.25 c.c.) of such a solution may be employed at one time.

In most cases of severe postoperative cystitis the writer has not used irrigations, but has depended chiefly upon internal therapy. Aspirin proved to be the most effective agent. Schlafl (Zeit. f. Gyn. u. Urol., Bd. ii, 4, 1910).

In most cases of very acute infection treatment must be limited to the administration of **abundant fluids** by mouth, **alkalies**, **sedatives**, and **urinary antiseptics**. Occasionally the intensity of the infection will require **drainage**, in which case the author advises suprapubic drainage with bladder instillations of **eusol** through Carrel tubes. Yet the value of urinary antiseptics is very doubtful, the most universally accepted drug being **hexamethylenamine**. Though bladder lavage is of value chiefly as a preliminary to the surgical treatment of enlarged prostate, stricture, tumor, calculus, etc., it is useless until the cause of the infection is ascertained. For lavage the author recommends **silver nitrate**, in a 1:20,000 solution at first and its strength then gradually increased. Vaccines are entirely

useless. Pyelitis will respond to the administration of **fluids and alkalis**, and **rest**. In recent years renal lavage with 5 to 20 per cent. **collargol** has been used for chronic pyelitis. Its value has yet to be proven. Dobson (Brit. Med. Jour., ii, 305, 1921).

Irrigations and injections of **permanganate of potash** in  $\frac{1}{12}$  to  $\frac{1}{4}$  per cent. solution is a most excellent remedy. In employing vesical irrigation it is important to observe the strictest attention to the cleanliness of all instruments used. Large injections should not be employed. Better an ounce or so at a time frequently repeated, until the washings come away perfectly clear. The temperature of the solution should be about 100° to 105° F. (37.8° to 40.5° C.). When there are local causes for reflex irritability, as hemorrhoids, varicocele, phimosis, adherent prepuce, or a narrow meatus, appropriate **surgical treatment** should be resorted to. Urethral causes of irritability of the bladder or of partial retention of the urine, such as stricture of either large or small caliber, should be attended to promptly (White and Martin).

The use of **cantharides**, even in the form of vesication, must be employed with caution in all forms of acute inflammation of the bladder, as cystitis is aggravated by its employment and may even be caused by its too free use, either internally or locally.

**Rest in bed** is of the most importance. **Large quantities of bland water** is a valuable remedy here, as in pyelitis. **Hexamethylenamine** in 5- to 10- grain (0.3 to 0.6 Gm.) doses is of value in the more recent cases. The **citrate of potassium** is valuable where the urine is too acid, while **boric acid** is of use to correct an alkaline urine. **Cantharidin**, 0.001 in 1 of alcohol, dissolved in 100 parts of water, may be given in

teaspoonful doses three to four times a day. Fluidextract of **corn silk** (*Zea mays*) in teaspoonful doses is useful.

Irrigations form the most important means of treatment at our command, and with irrigation it is well to combine distention of the bladder. The simple daily cleansing of the bladder in this way is of the utmost value, and many cases would recover rapidly if only bland fluids were used. The most efficient for this purpose are the **nitrate of silver**, 1:1500 to 1:500 or stronger, and **mercuric sublimate**, 1:1000.

As good a plan of administration as any is to connect a rubber tube with a funnel attachment to the catheter, and then slowly elevate the funnel two or three feet above the level of the pelvis. By the amount borne and the height the progress of the more difficult cases toward recovery can be pretty well estimated. The quality of great importance here for both patient and practitioner is patience. It sometimes takes weeks or months to secure the first decided step in advance, with many apparent setbacks in the interim.

*Direct Topical Treatments.*—When a cystitis is in the chronic stage, and is, furthermore, localized in a small area in the bladder,—one, for example, which could be covered by the last joint of the thumb,—direct topical treatments often hasten the improvement, and even effect a cure. The bladder is emptied, and the patient put in the knee-chest posture; then through an open cystoscope, using a head mirror or other suitable illuminant; the patch of inflammation is exposed and treated just as a chronic sore throat is handled, making a direct strong application by means of an applicator and a pledget of cotton. Here **nitrate of silver** is also best. It can be used over a small area, as strong as 50 per cent. For larger areas use 10 or 5 per cent., taking care that there is no excess of the solution to run down over the sound mucosa. Subsequent treatments must be milder, and at inter-

vials of from three to seven days. Solutions of 1 and 2 per cent. are often valuable in trigonal inflammation. Howard A. Kelly (Can. Pract. and Rev., Feb., 1906).

The following suppository at bedtime, will give a good night's rest:—

*R Extract of bella-*

*donna* ..... gr. iss (0.1 Gm.).

*Extract of opium*. gr. iij (0.2 Gm.).

*Cacao butter* .... q. s.

Mix and make 4 suppositories. (Amer. Jour. Clin. Med., Dec., 1908).

After **seminal vesiculotomy**, performed for the relief of the usual symptoms, mainly sexual, the writer noted that the cystitis, which is frequently associated with this disorder, cleared up. Cystoscopic examination of such bladders, showed that the cystitis was confined to the base of the organ, to that part of the bladder lying over the seminal vesicles. These inflammations are sometimes very extensive and occupy nearly the entire mucosa. The usual treatment of cystitis, viz., irrigations, drainage, etc., do no good in these cases; indeed they may even do harm. The only rational and effective treatment is seminal vesiculotomy. Eugene Fuller (Med. Record, Oct. 3, 1914).

The severe pain attending the passage of urine is often relieved by the use of 5-grain (0.3 Gm.) doses of **chloride of ammonium** every three hours, especially if litmus paper shows the urine to be acid.

For the excruciating pain and tenesmus of the early period of the acute trouble, nothing acts better than minute doses of **morphine**,  $\frac{1}{2}$  to  $\frac{1}{20}$  grain (0.005 to 0.003 Gm.), combined with **bromide of soda**, 5 to 10 grains (0.03 to 0.6 Gm.), and **hyoscyamus**, often repeated, but continued only under the supervision and direction of the physician. Such a prescription should not be left with the patient to have refilled *ad libitum*, lest he become a morphine habitué.

The best among the urinary anti-

septics are **salol** and **hexamethylenamine**. The former can be given in 5-grain (0.3 Gm.) doses three to six times a day, always with plenty of water. The latter is the better drug of the two, but it must be given with precaution. E. O. Smith (Lancet-Clinic, July 2, 1910).

In **chronic cystitis**, whatever be its origin, the treatment of the inflammation of the bladder should be by both local and internal medication until it is in a condition that will permit of more radical measures.

The next step is to remove the cause of the trouble, if discoverable. Strictures of the urethra must be dilated; foreign bodies must be removed; retention of the urine from enlargement of the prostate or paralysis, etc., must be treated by the regular use of the **catheter** and then by such operative interference as is deemed best suited to the individual case.

A soft catheter should be used and as often as the viscus will allow without adding to the irritability present, twice or three times in the twenty-four hours not being too frequent.

The author has employed graduated nickel **catheters** with a double or return flow, by which means the bladder is emptied of its contents, irrigation is employed, and the viscus, when contracted, is gradually enabled to hold larger and larger quantities of fluid, and by increasing the size of the instruments used the benefit of a sound is secured. After irrigating the bladder with these instruments, they are plugged, so that no fluid escapes, and allowed to remain in place for ten minutes. Considerable benefit has been derived from their employment.

The best internal remedies—i.e., those usually praised—are **benzoic acid**, about 30 grains (2 Gm.) a day in

divided doses; **benzoate of sodium**, 10 grains (0.6 Gm.) four times a day; **salol**, in a similar dosage, and **urotropin**,  $7\frac{1}{2}$  grains (0.5 Gm.) three or four times a day, well diluted with water. This drug, known officially as **hexamethylenamine**, is a most valuable remedy. Its beneficial action is believed to be due to the liberation of formalin in the urine.

Dudgeon claims that **hexamethylenamine** cannot be given in large enough doses to have any marked antiseptic effect in the bladder, but the clinical evidence does not substantiate his objections. Infusions of **linseed**, **buchu**, and **triticum repens** are often of value in acute cases. In the subacute stage, the oil of **sandalwood**, **cubeb**, and **copaiba** are most useful, but should not be employed for more than a few days at a time. In many cases, **salol** in doses of from  $\frac{1}{2}$  to 1 dram (2 to 4 Gm.) a day is more effective than hexamethylenamine. P. N. Pilcher (Med. Record, May 23, 1908).

From his investigations on the administration of **hexamethylenamine**, the writer concludes that there was no decomposition in either neutral urine or urine acidified with acid sodium phosphate in ten minutes, but in twenty hours there was evidence of slight formaldehyde formation in urine so acidified. This would indicate that to obtain formaldehyde liberation from hexamethylenamine the simultaneous administration of an acid-rendering substance is necessary, and *per contra* the compound should not be given with drugs in sufficient quantity to produce an alkaline urine. C. Williams (Lancet, May 18, 1912).

The balsamic oil of sandalwood, balsam of copaiba, oil of turpentine are to be avoided, as a rule, because they are badly borne by the digestive tract. Their administration is only advisable in gonorrheal cystitis, in which they are somewhat beneficial (Caspar, Leopold).

The patient should be advised to drink freely of water and should be careful regarding diet. Locally the bladder should be washed out once or twice a day with a solution of **permanganate of potash**,  $\frac{1}{4000}$  to  $\frac{1}{5000}$ ; **silver nitrate** in a similar strength; **boric acid**, 10 grains (0.6 Gm.) to the ounce (30 c.c.); **bichloride of mercury**,  $\frac{1}{4000}$  to  $\frac{1}{500}$ .

In cystitis due to enlarged prostate the question of operation has to be considered, and includes such procedures as **castration (White's operation)**; **resection of a portion of the vas deferens**; **enucleation of the prostate**; **incisions of the prostate (Bottini's method)**, etc.

For the radical cure of *infiltrating cystitis* and contracted bladder a **free incision** into the infiltrated tissues is the proper measure, similar to the incision into phlegmons elsewhere. Such an incision made in time will prevent the secondary shrinking of the bladder. The bladder is regularly cleared by **irrigations** with some indifferent aseptic fluid, and then the mucosa is treated by loosely packing the bladder with gauze saturated with a **silver** solution or with **ichthyol** and oil. This kind of tamponade is continued until the mucosa appears to be clean and until abnormal sensitiveness has completely disappeared. Then and not sooner the incision is permitted to close up.

Even after very extensive resections it is surprising to see, after everything is healed over and closed up, what a capacious viscus is again formed out of the remnants of the bladder. Though two-thirds of the organ is removed, a bladder will be reconstructed through the process of healing *per secundum* that will hold from 200 to 300 c.c. The explanation of this result can be found in the fact that healing by granulation furnishes a new roof for the bladder, built up of fibrous tissue, so that finally a

viscus is re-formed with almost normal capacity. G. Kolischer and H. Kraus (Surg., Gynec., and Obstet., July, 1910).

The writer recommends technique for the use of **iodine fumes**. The iodoform is placed in a spindle-shaped glass receptacle with an opening at the top and the open ends drawn out to permit a rubber tube to be slipped over each. As the iodoform is heated over an alcohol flame the fumes of iodine are pumped through a catheter into the bladder. He made 8 applications in a stubborn case of 23 years' duration, using 0.05 Gm. ( $\frac{1}{2}$  grain) iodoform each time. By the third, marked improvement was evident. All the symptoms subsided and there has been no further trouble during the two months since. He also had very gratifying results with it in the rebellious cystitis accompanying an enlarged prostate. The only caution is to keep the amount of air injected within the capacity of the bladder, previously determined. The applications seem to be best borne in the non-tuberculous cases. P. Cifuentes (Siglo Medico, June 30, 1917).

Anodynes are indispensable in many cases of cystitis to relieve the frequent desire to urinate and the extreme pain the patient suffers. They are best given per rectum and in the form of **opium** or its alkaloids. Whenever pain and strangury are absent there is, of course, no indication for their administration. Many cases demanding operation for the relief of the distressing symptoms inevitably associated with chronic inflammation of the bladder are only relieved by such measures as a **suprapubic cystotomy** or a **perineal section**.

There is generally ulceration in every case of painful cystitis. The pain in the majority of cases is due to ulcer, tuberculosis, or tumor, and treatment varies for each. Gen-

eral measures should be instituted, including prudent **tuberculin** treatment. There is no form of local treatment of a tuberculous bladder process that does not aggravate the disturbances. In the painful variety, the bladder will not tolerate even the ordinary technique of copious irrigation. The organ is actually a contracted bladder by this time, and will contain only a few cubic centimeters. A cystitis which becomes aggravated under treatment with **silver nitrate**, instead of showing a change for the better, is strongly suggestive of tuberculosis. **Corrosive sublimate** may have a favorable action, and use of small amounts of a 6 per cent. solution of **carbolic acid** has been recommended by Rovsing and is justifiable as a last resource. A mere **incision** into the bladder may have a favorable influence in some cases. The conditions for treatment are a little better with non-tuberculous ulceration; **silver nitrate** instillations may induce a complete cure if applied directly to the lesion with the aid of the cystoscope. **Radical removal of the ulceration** may be considered unless the lesion has progressed to an actual contracted kidney. In case of inoperable tumor, relief may be obtained sometimes from **injection** into the bladder of **warm olive oil**. If **mineral waters** are permitted they should be restricted to small amounts. Physical and dietetic measures are of the utmost importance, especially **local application of heat**, long **sitz baths**, and **avoidance of condiments**. **Milk** is the best beverage. Posner (Jour. Amer. Med. Assoc., from Berl. klin. Woch., Oct. 18, 1909).

**Vaccines**, especially the **autogenous**, have given good results in some instances; but the cases in which they have been tried have been too few to warrant an opinion as to their actual value.

Case in which a cystitis of eight years' duration had resisted all forms of treatment. **Bacterial vaccines** were then used, associated with **rest** in

bed for several weeks and weekly bladder irrigations, methods tried in vain before the vaccine treatment was begun. The urine, which always showed an abundance of pus (some of which had previously been inoculated into a guinea-pig to exclude tuberculosis), showed staphylococci, streptococci, and colon bacilli.

**Autogenous vaccines**, first of *Bacillus coli*, then of staphylococcus, and finally of streptococcus, were successful in eliminating all three varieties of bacteria, one after the other. From August to December 24th, weekly inoculations were given, at which time all symptoms had disappeared. During the month of January they returned to a slight extent. Another inoculation was given.

The patient has been absolutely free from pain or other form of discomfort and has been fully able to attend to her varied social interests. All pus has disappeared from the urine, and as far as one is able to

discover she is well. D. Fawcett (New England Med. Gaz., Jan., 1909).

**Vaccines** are of great value in the treatment of the acute cases in particular, and the writer urges the necessity for their employment at the earliest possible moment. **Tuberculin** is also of value in cases of tuberculous cystitis, but it is to be remembered here that the presence of the disease in one of the kidneys will render all local and general measures directed to the cure of the cystitis merely palliative, as the irritation is continually kept up with the certainty of reinfection. Newman (Lancet, March 2, 1912).

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**CYSTOSCOPY.** See URETERS AND BLADDER, EXAMINATION OF.

**CYSTOCELE.** See URINARY AND GENITAL SYSTEMS, SURGICAL DISEASES OF.

## D

### DAKIN-CARREL SOLUTION.

See SODIUM, AND WOUNDS, SEPTIC.

### DEAF-MUTISM.—DEFINITION.

Deaf-mutism, strictly speaking, signifies the abnormality which is characterized by the coexistence of deafness and dumbness. Various circumstances, which will be treated of in the following pages, necessitate, however, a more limited definition. Deaf-mutism may, therefore, be defined as a pathological condition dependent upon an anomaly of the auditory organs, either congenital or acquired in early childhood, causing so considerable a diminution of the power of hearing as to prevent the acquisition of speech, or—should speech have been acquired before the occurrence of the loss of hearing—as to prevent its preservation by the aid of hearing alone. Persons exhibiting

this pathological condition are described as deaf-mutes, even when speech has been acquired by a special system of instruction.

Theoretically, deaf-mutism is an ill-defined condition which cannot be distinctly separated from other conditions related to it. This is a natural consequence of its being a pathological term founded not only upon a symptom, deafness, but also upon the intensity of that symptom and the period of its occurrence. There is also an apparent contradiction in the fact that deaf-mutes include not only those who cannot, but also those who can, hear or speak somewhat. Practically, however, there is seldom any difficulty in determining whether a person is or is not a deaf-mute, just as it is, also, as a rule, easy to recognize deaf-mutism when the

subject in question has passed the first years of infancy. The reason is that the acquisition and preservation of speech in childhood is so dependent upon hearing that, as soon as the latter sinks below a certain degree, the former cannot be developed, or is lost, and this secondary dumbness does not easily escape observation. Occasionally it may be difficult to decide whether a child should be described as a deaf-mute or as merely deficient in hearing and speaking. Such cases must be decided by purely practical considerations, and it may not be out of the way to observe that in Denmark—one of the few countries where the education of deaf-mutes is compulsory—all children are considered deaf-mutes who cannot, owing to their deficient hearing, take part in the instruction given to normal children.

**CLASSIFICATION.**—Deaf-mutism can be classified (1) either according to the degree of its symptoms or (2) according to its etiology. In the first case a distinction must be made according as the deafness or dumbness is absolute or not. *True deaf-mutism* may be described as being the state in which the hearing is positively *nil*, and in which there is no power of speech, unless it be acquired by a special method of instruction. Persons with this form of deafness may be designated as true deaf-mutes. Those who have some slight power of hearing or some power of speech (either because the hearing is not totally absent or because the deafness occurred after speech had been acquired) may be described as *semi-mutes*.

Etiologically, deaf-mutism has been further divided into *endemic deaf-mutism* (i.e., that which attaches to certain districts and their natural conditions) and *sporadic deaf-mutism* (which

is the result of certain accidental causes).

The most general classification of deaf-mutism is that which discriminates between the deaf-mutism resulting from *congenital* pathological changes of the organs of hearing and that resulting from such changes which are *acquired* after birth.

We have reason to surmise, according to modern statistics, that at least half the cases of deaf-mutism are caused by acquired deafness. The relative proportion must, however, vary very much in different places and at different periods, epidemics of certain infectious diseases, for instance, increasing the absolute number of deaf-mutes with acquired deafness. Future investigations will, perhaps, prove that acquired deafness has a still greater preponderance in the causation of deaf-mutism than we are at present authorized in believing.

**DISTRIBUTION.**—We are only in possession of information as to the distribution of deaf-mutism in Europe, the United States of America, and some European colonies. Not even all European countries have undertaken an enumeration of their deaf-mute population, Russia, the largest of them, having, for instance, no deaf-mute statistics. The table shown on the next page gives the number of deaf-mutes in different countries; also the proportion of males and females.

It will be seen from this table that deaf-mutism is very variously distributed in the countries from which we possess statistics. The causes of the remarkably unequal geographical distribution of deaf-mutism, which will be seen from the table, are probably numerous and various. To begin with, we are involuntarily struck by the fact that the European countries with large deaf-

NUMBER OF DEAF-MUTES IN VARIOUS COUNTRIES.

Country.	Year.	Number of Deaf-mutes per 100,000 Inhabitants.	Total Number of Deaf-mutes.	Proportion Between Male and Female Deaf-mutes.
1. Switzerland.....	1870	245	6,544	100 : 74
2. Servia.....	1900	167	3,859	100 : 60
3. Hungary.....	1900	133	25,445	100 : 85
4. Baden.....	1900	115	2,147	100 : 79
5. Finland.....	1901	113	3,088	100 : 85
6. Austria.....	1905	109	29,505	100 : 81
7. Sweden.....	1900	108	5,289	100 : 79
8. Württemberg.....	1900	102	5,213	100 : 84
9. Italy.....	1901	96	31,267	100 : 81
10. Prussia.....	1900	91	31,448	100 : 84
11. Bavaria.....	1900	89	5,494	100 : 91
12. Roumania.....	1899	82	4,896	100 : 58
13. Hesse.....	1900	81	904	100 : 80
14. Norway.....	1900	80	1,767	100 : 85
15. Alsace-Lorraine.....	1900	78	635	100 : 91
16. Portugal.....	1878	75	3,109	100 : 73
17. United States.....	1900	68	51,871	100 : 90
18. Greece.....	1879	65	1,085	
19. Saxony.....	1900	57	2,396	100 : 83
20. Denmark.....	1901	57	1,390	100 : 75
21. Cape Colony.....	1890	53	802	100 : 78
22. Scotland.....	1891	53	2,125	100 : 78
23. British India.....	1901	52	153,168	100 : 65
24. France.....	1901	51	19,514	100 : 81
25. Ireland.....	1901	49	2,179	100 : 83
26. England-Wales.....	1901	47	15,246	100 : 85
27. Spain.....	1877	46	4,625	100 : 65
28. Holland.....	1889	44	1,977	100 : 82
29. Belgium.....	1905	30	2,005	100 : 95
30. Canada.....	1901	37	2,002	100 : 81

mute population are the most mountainous, which is in accord with the fact that deaf-mutism is—though with many exceptions—more frequent in mountainous than in lowland districts. I shall, later on, have occasion to point out that this is not, in all probability, the result of great altitudes and peculiar geological formations, but of the unfavorable social and hygienic conditions common to mountainous countries (consanguinity, poverty, unhealthy dwellings, etc.), the importance of which as causes of deaf-mutism will be discussed afterward. Further, widespread and malignant epidemics of cerebrospinal meningitis, an important cause of deaf-mutism, explain the frequency of this condition in some lowland countries of central Europe.

We must also observe that the countries in the west and south of Europe are

the most fertile and productive, while those in the north and center are less favorably endowed by nature. That this circumstance is a factor in the distribution of deaf-mutism has been proved by investigations made by me in different districts in Denmark, and especially by H. Schmaltz in Saxony. Finally, the northern and central countries are, on the whole, the most thinly populated in Europe, doubtless the result of the barrenness of the soil.

**SEX.**—The table opposite shows a greater frequency of deaf-mutism among males than females, the difference in several countries being considerable. The number of female deaf-mutes per 100 male deaf-mutes varies, according to the table, from 91 in Bavaria and Alsace-Lorraine to 58 in Roumania.

In the United States the proportion between male and female deaf-mutes was, according to the census in 1900, 100 to 90, while the corresponding figures in 1890 were 100 to 81. Also in other countries the proportion between male and female deaf-mutes varies much in different years. The numerical superiority of male deaf-mutes is the more remarkable, since females are more numerous than males in nearly all the European countries, Italy being the only country of those mentioned in the table which exhibits a slight inferiority as regards the female population. This numerical superiority of the male deaf-mutes must undoubtedly be considered principally as an expression of the greater liability the male organ of hearing has to be morbidly affected, combined with a greater mortality of female deaf-mutes.

**SYMPTOMS AND SEQUELÆ.**—Of the symptoms, the principal are, of course, deafness and dumbness; but other symptoms closely connected with



the ear disease causing deafness are often met with in cases of deaf-mutism.

**Deafness.**—The term “deafness” is not only used to express the absolute absence of hearing—total deafness—but also to express a condition in which some traces of hearing remain, but in which the human voice is not audible in the usual way: a condition to be described as partial deafness. From a theoretical point of view, it seems an easy matter to make a sharp distinction between the condition in which the auditory nerve is entirely out of function and that in which it still acts, though deficiently. As a matter of fact, however, it has been proved that it is sometimes difficult to decide, in particular cases, whether there are any remains of hearing or not, and, further, the results of these two conditions (if acquired in early infancy or congenital) are the same, viz.: deaf-mutism. In other words, both subjects with total deafness and those with partial deafness may be met with among deaf-mutes.

It is not always an easy matter to test and decide the amount of hearing possessed by a child, especially an infant. As a rule, only ordinary loud sources of sound can be employed to discover whether the child in question reacts in any way to the sound produced; for instance, by turning or blinking its eyes. Generally, a loud whistle, a bell, clapping the hands, or such like devices are made use of. Such a rough mode of examination can, however, only decide whether the power of hearing exists or not in individual cases, and even this is often difficult when the patient is an infant, and it is also no easy matter to determine whether the power of hearing is equal on both sides. With older children it is easier to discover whether the power of hearing exists, and, if so, in

what degree. In the latter case less powerful sources of sound may be employed. Of these the principal is the tuning-fork, the vibrations of which are used in measuring the conduction of sound through the middle ear, by placing it outside the ear, and also in measuring the so-called bone, or craniotympanic, conduction, by placing it on the mastoid process or on the teeth. The human voice is also an important means of investigation. The best means of employing it is by pronouncing certain vowels loudly and distinctly close to the deaf-mute's ear, without his being able to see the movement of the lips, the patient being asked to repeat the vowels pronounced. To prevent the possibility of guessing, the vowels should be repeated several times. If the deaf-mute understands the vowels easily, consonants and even words and short sentences may be tried. In most cases this method can only be made use of when the deaf-mute in question has learned to articulate. A greater power of hearing is seldom met with, unless sound-increasing apparatus are employed. The hearing of deaf-mutes with considerable remains of hearing can also be tested with a loud-ticking watch placed outside the ear or pressed against the outer ear. It is, however, very unusual for deaf-mutes to be able to distinguish the high notes represented by the ticking of a watch. In employing all these methods, it must be remembered that the hearing of deaf-mutes differs greatly at different times in some cases, according to varying conditions in the ear, of which we have no immediate knowledge.

The reports of various investigators, as to the relative number of deaf-mutes with total deafness, differs considerably, for, while some have found that only about one-fifth of the deaf-mutes ex-

amined were totally deaf, others have found a much larger proportion, the principal cause of this discrepancy being probably the fact that there is generally a distinct relationship between the deafness and its cause. This relationship is most distinctly seen by comparing the power of hearing of congenital deaf-mutes with that of deaf-mutes with acquired deafness. All investigators, with but a few exceptions, have found a much greater number of cases of total deafness among deaf-mutes with acquired deafness than among deaf-mutes with congenital deafness.

The fact that so many more cases of total deafness are met with among deaf-mutes with acquired deafness than among those with congenital deafness is a proof that postnatal processes in the ear, causing deafness, are much more destructive than the same processes occurring during fetal life. Most authors have also found that congenital deaf-mutes are more frequently in possession of a considerable degree of hearing (hearing of vowels or even of words) than deaf-mutes with acquired deafness.

It may be mentioned, finally, that Bezold examined the hearing power of deaf-mutes by means of a graduated series of tuning forks, and found that frequently "islands" of perception of notes alternated with total defects of hearing. These defects appeared most frequently in the lower end of the scale—a fact which has been corroborated by Uchermann.

**Mutism.**—Mutism was in early times believed to be the primary and essential symptom of deaf-mutism, but it is known now to be a secondary phenomenon which is the consequence of the deafness. That this is the case is also evident from the fact that the degree of mutism is, as a rule, in exact relation to

the degree of deafness, and also to the period at which the deafness makes its appearance. Thus congenital deafness, or deafness acquired in early infancy, is always accompanied by complete mutism (excepting in cases in which the mutism is removed by special methods of education), while in cases of acquired deafness, in which the deafness is either not total or arises after the child has learned to speak, a certain degree of speech is respectively acquired or retained. The explanation is simple, speech being, under normal circumstances, acquired through the ear, the child imitating the words which it hears spoken by those about it. It may, however, be mentioned that even children totally devoid of hearing produce sounds which sometimes resemble words, such as "ma-ma," "ba-ba," etc., and sometimes also imitate animals, often thus causing their parents to suppose that they are capable of hearing. This may be because the above-mentioned sounds and the voices of certain animals are produced by very simple movements of the vocal organs which can be imitated by spontaneous observation. Finally, it is possible that the vibrations caused by such loud sounds as the barking of a dog, bellowing of a cow, etc., may be perceived by the aid of touch, which sense is often highly developed in deaf children, and consequently guides them in imitating the sounds.

The question as to the degree of deafness which must exist, or, in acquired cases, the age at which the deafness must appear in order to cause mutism resulting in deaf-mutism, cannot be answered decidedly. To begin with, the application of the term "deaf-mutism" is entirely arbitrary in cases in which there is some power of hearing or of speech, and the distinction between a

deaf-mute child and a child with deficient power of hearing must, in some cases, depend entirely upon practical considerations, of which the method of instruction which is requisite for the child's education is, as a rule, decisive. Thus, for instance, a child of well-to-do parents who is able to hear tunes and, to a certain extent, reproduce them will scarcely be considered deaf and dumb and sent to an asylum, while a child with the same degree of hearing, but of poor parents, will be treated as a deaf-mute because the parents are unable to give it the special education which it requires. The non-development or deficient development of the power of speech in cases of congenital partial deafness and its complete or partial loss in cases of acquired deafness are also often dependent upon the assiduity with which a child's friends attend to its development or preservation. Some children, too, seem to have a greater aptitude for developing or retaining the power of speech than others; and this seems to be not only dependent upon their intellectual faculties, but also upon other unknown conditions. Thus, a child with comparatively very slight power of hearing, or with deafness acquired soon after birth, may exhibit a comparatively considerable power of speech, while another child with greater powers of hearing and later acquired deafness may be entirely without it.

Future investigations will, in all probability, decide how far total acquired deafness results in total mutism. Hartmann states that deafness acquired before the age of 7 causes secondary mutism, and this opinion is, no doubt, correct. On the other hand, there are reports from various places to the effect that deaf-mutism may appear at the age of 14 or 15, or even later. In these

cases, however, it is probable that the term deaf-mutism is incorrect, though, of course, such accidental circumstances as feeble-mindedness, blindness, etc., may necessitate the registration of persons who have lost the power of hearing so late in life as deaf-mutes, because they are unable to read from the lips, or unable to pronounce so distinctly as to be understood.

As mentioned above, mutism in deaf-mutes may be either total—*i.e.*, the power of speech may be entirely wanting—or it may be partial, in which latter case the power of speech is developed, or, in acquired deaf-mutism, it is retained to a certain extent. This power of speech is frequently considerable; so that such persons cannot, properly speaking, be termed mutes. There are, however, certain peculiarities which always attach themselves to the speech even of persons who are only partially deaf from their birth, or who have become deaf during childhood. These peculiarities, which are still more pronounced in true deaf-mutes, consist in the absence of accentuation of syllables and of words, the result being that speech becomes monotonous. Besides this, the speech of such persons is generally dull-sounding and feeble, and the control of respiration is also deficient. The stock of words is also sometimes limited, though this peculiarity is, under ordinary circumstances, not very noticeable, excepting in cases where the power of hearing is very slight, or where the deafness appears comparatively early. These physical deficiencies in the speech of deaf-mutes are easily accounted for, because the power of hearing is not only important in the development of speech by enabling a child to imitate the speech of others, but it also enables it to regulate the modulation, sound, and force of

its voice by the aid of the vibrations which reach the labyrinth through the bones of the cranium.

The power of hearing plays so great a part in the above-mentioned physical qualities of speech that its loss cannot be completely compensated for by any other sense. It is, however, possible, by aid of sight and touch, to teach a great number of deaf-mutes to speak well enough to be able to use speech as a means of communication. Persons who have been totally deaf from birth can also be taught, by a special method of instruction, to speak so that they can be understood, though with the peculiarities above mentioned. Owing to these peculiarities, such speech has received the name of "articulation." It is not always an easy matter for the deaf-mute to retain the power of speech which he has gained with so much difficulty, when he enters the world and comes in contact with persons who cannot, or can only partially, understand him. In such cases the deaf-mute generally abandons the use of speech as a means of communication, especially as lip-reading requires great attention and well-developed sight.

#### **Disturbances of the Equilibrium.—**

It has been mentioned that acquired deafness is often accompanied by disturbances of the equilibrium, both at its first appearance and immediately afterward, and that this complication is most frequent in cases where the deafness has been caused by cerebrospinal meningitis. Mention is also made in literature of some few cases of congenital deafness accompanied by disturbances of the equilibrium, consisting in uncertain and staggering gait, both during the first years of childhood and later on in life. James was the first to draw attention to "immunity from dizziness," under circumstances which otherwise produce

dizziness and consequent disturbance of the equilibrium, as characteristic of deaf-mutes. He examined altogether 519 deaf-mutes, and found that 186—*i.e.*, 36 per cent.—did not feel the least dizziness when spun around rapidly, no matter in what position their heads were placed. James was also informed by many of these deaf-mutes that they experienced a remarkable feeling of helplessness and want of sense of locality when under water, several of them also stating that these sensations were unknown to them before the loss of hearing. Kreidl endeavored to discover in a more rational manner, and by the aid of a specially constructed apparatus, an objective proof of the above-mentioned phenomena in deaf-mutes, and also to decide their nature and strength. Pollak endeavored to produce dizziness in a number of deaf-mutes by conducting a galvanic current through their heads. Several exhibited signs of dizziness, accompanied by movements of the head and eyes; also exhibited by normal subjects under like circumstances, while 29.3 per cent. were not affected in any way; in these, then, it was to be supposed that the semicircular canals were entirely destroyed, and Pollak points out the resemblance between the figures thus obtained and the percentage of cases of entire absence or destruction of the semicircular canals found by post-mortem examination of deaf-mutes.

Other investigators have later proofs of the existence of these disturbances of the equilibrium in deaf-mutes caused by partial or total destruction of the static part of the internal ear. Barony has quite lately found a new and trustworthy way of examining the static function of the labyrinth by means of syringing the ear with cold or warm water, which produces a certain form

of nystagmus when the static part of the internal ear is not destroyed, while no nystagmus is produced in cases where the static apparatus is destroyed. There is no mistake that this way of examining the static function of the labyrinth will give similar results in deaf-mutes to those described above.

Although deaf-mutism brings with it a long train of indirect consequences, which are of great importance as affecting the daily life of the deaf-mute, its more direct results are but few, and even these are the subject of dispute.

**Deficient Development of the Mental Faculties.**—There can be no doubt that the want of such an important sense as hearing must, at least, result in a slow development of the mental faculties, as the psychological function of the brain develops not only in proportion to its receptivity to impressions from without, which are so necessary for mental growth (*"nihil est in intellectu quod non antea fuerit in sensibus"*), and to the quality of these impressions, but also in proportion to their quantity, which must of necessity be diminished when one of the routes by which they reach the brain is closed or partly closed. This does not, of course, prevent a deaf-mute from attaining the same degree of intellectual development as a normal person with the same amount of intelligence, if his physical deficiency is compensated for by energy, industry, etc. There is, however, no doubt that purely practical considerations—for instance, the necessarily limited choice of professions—often hinder such a complete indemnification for the loss of so important a sense as hearing. The deaf-mute is thus deprived of one of the most important incentives to energy,—namely, ambition, and it is, doubtless, in these

external hindrances that the reasons are to be sought why no deaf-mute has as yet written his name on the pages of history. Further, the morbid processes causing deaf-mutism often have their seat in the brain, as has been already pointed out, and these processes often leave other traces behind them. Hartmann found also that one-half of the pupils examined by him in deaf-and-dumb asylums, whose deafness was due to brain disease, were but moderately or indifferently endowed with intelligence, and it was altogether doubtful whether many of these subjects were capable of instruction. There are also statistical proofs from other countries that deaf-mutism is often accompanied by want of mental power. It is not, however, correct to infer that deaf-mutism can result in idiocy from the circumstance that deaf-mutes are often idiots. Idiocy, when it appears simultaneously with deaf-mutism, is the result of a congenital brain disease, or one acquired in infancy, and is of superior or co-ordinate importance to the deaf-mutism itself; persons exhibiting both these abnormalities must, doubtless, not be considered as idiotic deaf-mutes, but as deaf-and-dumb idiots. H. Schmaltz and Lemcke have made some measurements of the heads of deaf-mutes in order to elucidate the question as to the intelligence possessed by deaf-mutes. Both these investigators found that the heads of deaf-mute children were, as a rule, smaller than the heads of normal children, especially in the younger age periods. The reason is, doubtless, that the mental faculties of deaf-mute children are less developed than those of other children.

**Abnormalities of the Ear Found by Objective Examination.**—While the section of this paper on morbid

anatomy will be mainly devoted to the pathological changes of the deeper parts of the ear, it is my purpose, under this heading, to deal with the abnormalities found in those parts of the ear which are accessible to objective examination. It would naturally be supposed that, as deaf-mutism is often caused by anomalies of the ear, deaf-mutes would often exhibit congenital abnormalities of the external ear. This is, however, not the case, as congenital malformations of the external ear are but seldom met with. A close investigation of the cases of malformation of the external ear reported in literature proves also that these abnormalities are but very rarely accompanied by such a diminution of the powers of hearing as to result in deaf-mutism, which circumstance has been laid much stress upon by Toynbee. Abnormalities of the external meatus have been often met with. It is, however, often difficult to decide the nature of the abnormalities from the descriptions of them we possess, and a comparison of the frequency with which they have been found by various investigators is, therefore, of no interest. Contraction of the meatus would seem to be the abnormality most frequently met with. The greatest interest, however, attaches to the closing of this passage, which has been found by many investigators without being accompanied by any malformation of the external ear. There can be little doubt that when the meatus is closed by a membrane situated close to the external ear this is due to congenital malformation; should the membrane, however, be situated deeper in the meatus, it is possible that the obstruction is the result of inflammation in the tympanic cavity. I have, at least in several cases, observed such a closing of the external

meatus of deaf-mutes resulting from scarlatinal inflammation, in the one case on both sides; in the other on one.

As to otoscopic examinations of deaf-mutes, these have contributed very little to the pathogenesis or etiology of deaf-mutism. Such investigations have been published by various authors, whose researches, in spite of the care which has been bestowed upon them, have led to very little result; in fact, the various authors differ very considerably in the results obtained. The difference observed in the results of examinations of normal children and pupils at deaf-and-dumb asylums lies in the greater frequency with which the abnormalities found appeared in deaf-mutes, and not in the nature and kind of these abnormalities. All investigators who have classified the deaf-mutes examined by them according to the nature of their deafness (congenital, acquired, or doubtful) agree that the otoscopic examination of the drumheads in cases of congenital deafness yields a negative result more frequently than in cases of acquired deafness, the latter more frequently exhibiting destructive inflammatory processes or the traces of such.

**Abnormalities of the Mucous Membranes Adjacent to the Ear.**—Catarrhal changes of the mucous membranes of the nose, nasopharynx, and pharynx have been frequently observed. These changes have most frequently taken the form of hypertrophy of the whole mucous membrane, or of the adenoid tissue (adenoid vegetations, hyperplasia of the tonsils), less frequently the form of atrophy (ozena, atrophic catarrh of the nasopharynx and pharynx). The frequency with which catarrhal changes of the upper air tract have been observed by investigators differs greatly. The cause is doubtless to be sought in

the circumstance that catarrhal diseases of the nose, nasopharynx, and pharynx appear with varying frequency in different countries and in different classes of society, as climate, mode of living, clothing, hygienic conditions, etc., as is well known, play an important part in the appearance of catarrh in the air passages. The results of such examinations of deaf-mutes will, therefore, first be of use in judging of the relation of such affections to deaf-mutism, when we possess information as to the frequency with which catarrhal diseases of the upper air passages appear in normal subjects of the same age and living under the same conditions as the deaf-mutes from which to draw comparison. It seems, however, to be beyond doubt that deaf-mutes suffer with great frequency from adenoid vegetations of the nasopharynx.

**Abnormalities of the Eye.**—Although we find several notices of abnormalities of the eyes of deaf-mutes, it is often difficult to decide whether these are accidental phenomena or connected etiologically with deaf-mutism. Among the abnormalities of the latter category may be mentioned retinitis pigmentosa, various malformations of the eye; atrophy of the bulb caused by panophthalmia, a result of the same acute disease as caused the deafness; finally syphilitic interstitial keratitis.

**DIAGNOSIS.**—Although deaf-mutism from a theoretical point of view is not a very distinctly defined condition, still the majority of cases are easily recognized. The question whether a person is a deaf-mute or not must, according to what has been laid down in the foregoing pages, be principally decided by examinations as to the function of the auditory nerve. If this is entirely suspended, or so reduced that speech

cannot be heard, and if the history of the case proves that this condition dates from birth or infancy, then the subject must be regarded as a deaf-mute. We are also justified in applying this term, as has already been pointed out, even where there exists some power of speech, either acquired by special means of instruction or where the deaf-mutism has appeared at a more advanced age, retained to a greater or less extent. The circumstance that the pathological condition called deaf-mutism is based upon a symptom the extent of which cannot be measured with any degree of certainty, but which, nevertheless, is decisive, naturally causes arbitrary decisions in some cases, which decisions generally depend upon purely practical considerations. In other words, there are persons as to whom it is difficult to say with certainty whether they are deaf-mutes or not. Such are persons who can hear the human voice to a certain extent, and who consequently learn to articulate by the aid of special methods of education, or such as have lost the power of hearing so late that they have retained the power of speech, although their voice is always somewhat peculiar. Such persons are, however, but few in number, and consequently the difficulty in diagnosing deaf-mutism mentioned here is of very slight practical importance.

Of much greater importance are the difficulties which present themselves when the person in question is an infant. It must, however, be pointed out that the term "deaf-mute" is incorrect when applied to children under a year old, as no children can speak at that age. It would seem, indeed, that great caution must be observed in drawing the conclusion that deaf-mutism will necessarily be the result of even total deafness ob-

served during the first year of infancy, since, according to the experience of many investigators, there are some children who are unable to react, or who react very slowly, to sounds during the first year of infancy, but whose hearing, nevertheless, when older, is perfectly normal. In any case it is extremely difficult to arrive at any decided opinion whether an infant possesses the power of hearing or not, and especially as to what degree of hearing it possesses, and, as a rule, the younger the child, the greater is this difficulty. The reason is, doubtless, that the sound-conducting apparatus of infants is not complete at birth. The external meatus and the tympanic cavities are transformed after birth from cavities filled with cellular tissue to pneumatic cavities. It was formerly supposed that infants did not react to sound, but it has been proved that this is not the case, even with newborn infants, and infants can also perceive musical notes. Even in the second half of the first year of childhood it is, however, very difficult to decide whether the power of hearing exists or not. No great confidence can be attached to the statements of a child's parents or friends as to its having heard certain sounds, as the vibrations of the air caused by certain sources of sound may produce effects upon the sensory nerve which may be mistaken for the result of vibrations of air acting upon the auditory nerve. It is, therefore, of the greatest importance, in experimenting with the hearing of infants, to make use of such sources of sound, or to make use of them in such a manner that only the vibrations of sound produced can be perceived. Loud dinner-bells are suitable for this purpose; the so-called watchman's whistle, low notes of Galton's whistle, clapping of hands, and the

firing of small pistols, which the child should not be allowed to see. If the child reacts to these sounds it will blink its eyes or exhibit either joy or fear.

Should the results of such experiments be negative, it is not necessary, as before mentioned, to conclude that the child will become a deaf-mute. After the completion of the first year of infancy, however, the older the child, the greater the importance which must be attached to such negative results. After that period we may look for another symptom to help us in our diagnosis, viz.: the absence of speech. This, too, may be delusive, as some children, although in full possession of normal powers of hearing and intellect, do not begin to speak at the end of their first year, but later, sometimes much later. The cause may be some hidden condition or constitutional disease; for instance, rickets.

Another condition which may be mistaken for deaf-mutism is simple mutism (aphasia) uncomplicated with deafness or idiocy. This abnormality, which is not at all rare in adults as the result of certain brain diseases, is but seldom congenital or acquired in infancy. This form of aphasia must, according to some authors, be regarded as the result of a disease which is localized in the central nervous system, causing total inability of speech in the person affected or inability to speak more than a few indistinct words. This infantile aphasia, which seems, as a rule, to be congenital, differs from the mutism of deaf-mutism, principally inasmuch as it is not accompanied by deafness, and often, also, in the subject affected being able to produce certain words or sounds resembling words, which are always employed in attempts at speech. Aphasia accompanying feeble-mindedness, imbe-



cility, or idiocy is a much more frequent abnormality, which is still more easily mistaken for deaf-mutism, especially in such cases where the imbecility is so considerable that the interest for sound is diminished. In these cases, however, the imbecility, which must be regarded as the primary disease, will generally show itself in the patient's appearance, movements, gestures, etc.

Hysterical mutism may sometimes simulate deaf-mutism. It is, however, generally accompanied by pronounced symptoms of hysteria, and exhibits itself by the patient's making no attempts to speak, or even to articulate. It is generally of short duration and easily recognized, the diagnosis only offering some difficulty in cases where the mutism appears in deaf, hysterical subjects.

The question whether deaf-mutism is congenital or acquired is, doubtless, that which offers the greatest difficulty in forming a diagnosis of deaf-mutism. In all cases, however, when the deafness appears after the child has begun to speak, or where the immediate causes of deafness are known, the diagnosis is an easy matter. If, on the contrary, the deafness has made its appearance prior to the period at which speech is generally developed—whether the morbid changes of the organs of hearing causing deafness are congenital or acquired—a decision as to the fetal or postfetal origin of the deafness is accompanied by great, indeed often insurmountable, difficulties. In such cases it is, therefore, of the greatest importance to obtain the most explicit information from the deaf-mute's friends, especially the parents, who are most likely to be able to give reliable information as to the diseases and pathological conditions which exist in the family. An opinion as to the origin of deaf-mutism can, as

has been previously mentioned, only in exceptional cases be based on objective examination of the subject. Such exceptional cases are, for instance, those in which visible and pronounced malformations of that part of the ear which is accessible to examination clearly indicate that deaf-mutism is the result of congenital changes of the auditory organs. Such cases are, however, very rare. Malformations in other parts of the body also indicate, though with a much less degree of certainty, that the condition in the ear is congenital; but these cases are rare. The objective examination of the ear, in the great majority of cases, offers nothing which can be relied upon with any degree of certainty, since, on the one hand, pathological changes of the external and middle ear, which may, according to their nature, be acquired after birth, may very well exist in persons whose deafness is due to congenital malformations of the auditory organ; while, on the other hand, less pronounced congenital changes of the external and middle ear (for instance, lesser degrees of microtia and macrotia, contraction of the external meatus, abnormal position of the drum-head, etc.) may very well appear in persons with acquired deafness.

Deaf-mutes do not seem to feel anything tickling the inside of their outer ear, while children with a normal hearing apparatus feel the tickling at this point with exceptional intensity. The writer introduced a bougie into the ear and twisted it to and fro and found that this was borne without a trace of shrinking by 94 children in a deaf-mute asylum, although all were extremely ticklish elsewhere. On the other hand, 50 normal children tested in the same way felt the tickling with special intensity, though most of them otherwise were not especially ticklish. This test is useful for differentiating

actual deaf-mutism from mutism due to other causes, with or without hearing. Treatment based on the findings has given good results in 12 children, idiots and others, supposed to be deaf-mutes. Fröschels (Med. Klinik, Dec. 25, 1910).

A final decision as to the congenital or acquired origin of a case of deaf-mutism must, then, in the majority of cases, be entirely based upon inquiry, and, even when explicit information is obtainable, it is often difficult to arrive at a definite opinion. It will be always advisable to make inquiries whether the child's speech has developed in the same way as that of ordinary children of the same age, because non-professional persons' statements as to a child's power of hearing are often unreliable. Should the answers be in the affirmative, and should it be proved that the power of speech has been lost, or is arrested in its development from some or other cause (acute brain disease, scarlet fever, measles, etc.), it may be safely concluded that the deaf-mutism is of post-fetal origin. This diagnosis is also justified, though with less certainty, when the above-mentioned causes have shown themselves during the first years of infancy, unless, of course, ample and satisfactory proof can be produced that the child has never possessed the power of hearing, or that the more remote causes of deaf-mutism (unfavorable social conditions, heredity, consanguinity, etc.) have appeared in great force; in such cases a decision must remain doubtful. Should, however, the possibility of the direct causes (scarlet fever, brain diseases, measles, etc.) be excluded, and it is proved that the child never possessed the power of speech, it may be supposed that the deaf-mutism is the result of congenital changes of the organs of hearing. This supposition is

the more warranted the greater proof there is that the more remote causes of deaf-mutism have played their part in the case in question.

**ETIOLOGY.**—The causes of deaf-mutism may be subdivided into two groups: (A) the remote causes, and (B) the immediate causes.

(A) **Remote Causes.**—Among these are to be mentioned principally natural conditions, unfavorable social and hygienic conditions, heredity, consanguinity, and a few others of minor importance.

*Natural Conditions.*—In considering the unequal distribution of deaf-mutism we are involuntarily led to the supposition that this phenomenon may be caused by varying natural conditions, among which soil and elevation seem to play an important part.

To H. Schmaltz is due the honor of having investigated the question of the importance of geological conditions and elevation in Saxony so thoroughly that his results are entirely to be relied on. In these investigations, which have embraced the minutest details which could possibly be of importance concerning the appearance of deaf-mutism, the author has weighed each separate point carefully. His conclusions are as follows: There is nothing to be said in favor of the hypothesis that soil, climate, or other territorial conditions influence the deaf-mute rate, neither can the composition of the water be proved to affect it in any way, but it is the social and hygienic conditions which are decisive. Lemcke, in Mecklenburg-Schwerin, and Uchermann, in Norway, were also unable to prove that geological conditions are a cause of deaf-mutism.

*Unfavorable Social and Hygienic Conditions.*—Almost all authors who have considered the question of the

connection between deaf-mutism and unfavorable social and hygienic conditions agree in ascribing to them great importance as causes of deaf-mutism. The statistical proofs in support of this hypothesis are not, however, on the whole, very satisfactory. The best statistics are furnished by H. Schmaltz, who has come to the following conclusions: "The industrial population, and especially that part of it which is worst off pecuniarily,—in fact, all who are in danger of degenerating both morally and physically on account of insufficient means, or poverty, and who, consequently, are unable or unwilling to take the necessary care of their children,—all such persons exhibit the highest percentage of deaf-mutes among their descendants. Finally, when, in addition to all these unfavorable conditions under which children are born, they are brought up by a family which, from various reasons, is, perhaps, more or less degenerated, and have to undergo all sorts of diseases in infancy without having sufficient power of resistance, thus deaf-mutism is an only too common result." On the other hand, Uchermann states that in Norway unfavorable social and hygienic conditions are far from increasing the deaf-mute rate, it being higher among the better situated classes.

*Heredity.*—Opinions have differed greatly as to the heredity of deaf-mutism, the reason being that not only are the laws which govern the hereditability of pathological changes and diseases subject to different interpretations, and that the statistics employed have given different results, but also that the term "heredity" is used in different ways.

The term "heredity" is used by many authors to express the frequent appear-

ance of the same pathological condition in two consecutive generations, other influences having, of course, been excluded. The statistics which have been employed in attempts to solve the question of the frequency with which deaf-mutism appears in two consecutive generations have been based on two different methods: the one calculating how often deaf-and-dumb persons had deaf-and-dumb parents, the other how frequently unions where the one or both parties were deaf and dumb resulted in deaf-and-dumb offspring.

The first mode of ascertaining the frequency with which deaf-mutism appears in two generations, consisting in discovering how often deaf-and-dumb subjects belonging to large groups of deaf-mutes are descended from deaf-and-dumb parents, everywhere gives the result that deaf-mutes very seldom have deaf-and-dumb parents. This is even the case when only congenitally deaf have been the objects of investigation, Uchermann, for instance, finding in Norway among 921 deaf-mutes with congenital deafness only 2 with deaf-and-dumb parents. This seems to prove that deaf-mutism is rarely inherited in the strictest significance of the term, or, as it might also be expressed, inherited directly. It must, however, be borne in mind that marriages contracted by deaf-mutes are, and especially have been, comparatively rare in Europe, and also that their fertility is smaller than that of other marriages; there can certainly be no doubt that the direct hereditability of deaf-mutism is certainly of much greater importance than might be supposed from the above-mentioned statistics.

This opinion is corroborated by statistics founded on the second mode of estimating the frequency with which

deaf-mutism appears in two consecutive generations, viz.: by calculating how frequently unions where one or both parties are deaf and dumb result in deaf-mute offspring. The European statistics of this kind are but few and small, the reason being mentioned above, while the excellent American statistics collected by E. A. Fay are very comprehensive, marriages contracted by deaf-mutes being so much more frequent in the United States. The principal results of European statistics have been that a deaf-and-dumb child was born in about every thirtieth or thirty-first union where one party was deaf and dumb, and that deaf-mute offspring were much more frequently the result of unions where both parties were deaf and dumb. The statistics published by Fay are based on investigations of over 5000 marriages contracted by deaf-mutes, and have given the result that over 9 per cent. of these resulted in "deaf offspring, and, curiously enough, the marriage where both parties were deaf did not result more frequently in deaf offspring than those where only the one party was deaf." Fay also found that marriages of congenitally deaf persons and of deaf persons with deaf relatives gave a far greater liability to deaf offspring.

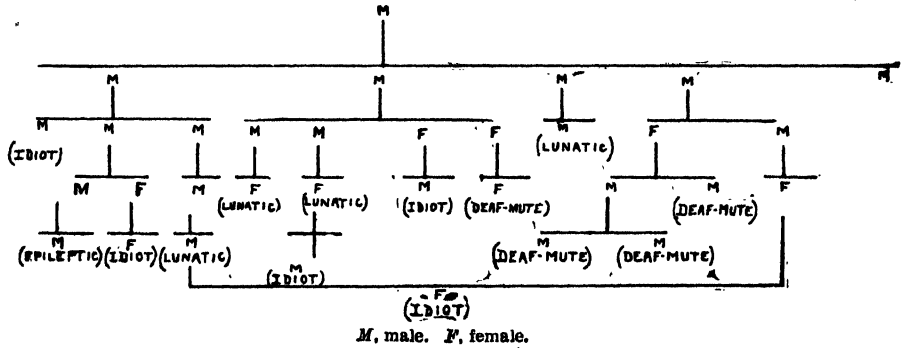
If, now, the term "heredity" is used to express the conspicuous frequency with which the same abnormality appears in the same family, the hereditability of deaf-mutism becomes still more evident. The frequency with which deaf-mutism appears among the parents of deaf-mutes has been mentioned above. Cases of deaf-mutism among the grandparents, great-grandparents, etc., of deaf-mutes, which should prove the direct heredity *per saltum*, as it is termed, must necessarily be still less

frequent, as marriages between deaf-mutes were very rare in the first half of this century. If we, however, look for cases of deaf-mutism in other branches of the deaf-mutes' family tree, we find in all statistics that—considering that deaf-mutism is a comparatively rare pathological condition—a great number of deaf-mutes are to be found among the uncles, aunts, great-uncles, great-aunts, cousins, and second cousins of deaf-and-dumb persons. According to European statistics, embracing a large number of deaf-mutes, about every sixteenth deaf-mute has one deaf-and-dumb relative among the category above mentioned (parents, grandparents, brothers, and sisters excepted), the point where deaf-mutism most often appears corresponding to generations co-ordinate with the parents. These statistics have also shown that it is almost exclusively congenital deafness which plays a part in this respect. Deaf-mutism, finally, is to be met with more frequently among the brothers and sisters of deaf-mutes, and there are statistics as to congenital deaf-mutes according to which 50 per cent. of these had one or more deaf-and-dumb brothers or sisters. The appearance of deaf-mutism in two or more children of the same parents is very characteristic, and there are few pathological conditions which show such a tendency to appear in the same branch of a family, there even being cases on record where ten deaf-and-dumb children were born in the same marriage.

Finally, if by heredity we understand the frequent appearance in a family of not only one pathological condition, but of several others related to it anatomically or etiologically, we shall see that heredity is a most important factor in the etiology of deaf-mutism. It is,

namely, proven by several comprehensive statistics that partial or total deafness due to different ear diseases (which have not led to deaf-mutism, on account of the lesser degree of the loss of hearing, or of its unilateral appearance, or of its later development in life), insanity, epilepsy, idiocy, stammering and other defects of speech, hysteria, and several other nervous diseases appears with conspicuous frequency among the relatives of deaf-mutes and with about double the frequency among the relatives of congenital deaf-mutes as among the relatives of deaf-mutes with acquired deafness.

congenital and the acquired, the latter, of necessity, including numerous cases in which deafness is to be traced to accidental causes, is alone sufficient to render the interpretation of the laws of heredity, by the help of investigations which embrace deaf-mutes in general, of the greatest difficulty. When we add to this that, although the importance of heredity in deaf-mutism is undoubted and considerable, there are other factors of at least equal importance, and that there is much which tends to neutralize the transmission of morbid tendencies (favorable social conditions, crossed marriages, etc.), it will be evident that



Their appearance is particularly clearly demonstrated by several genealogical tables published by Dahl and Uchermann, of which the one depicted above is an interesting example.

The laws which may, then, be supposed to regulate the heredity of deaf-mutism are difficult of interpretation, and seem, in many respects, to differ from those which relate to other pathological conditions and diseases. This may be accounted for by supposing that, as the causes of deaf-mutism in general are numerous and varied, so are also the causes of each individual case. The circumstance that deaf-mutism, so far as its etiology is concerned, must be divided into two distinct classes, the

there is much which renders a just explanation of the laws of heredity anything but an easy task. If we compare deaf-mutism with hemophilia, which it resembles so far as heredity is concerned, we shall see how correct the above statements are. Hemophilia—which, like deaf-mutism, may pass over several generations and accumulate in a single, being also most frequent among males and in the children of fruitful marriages—is, etiologically, but little complicated, partly because it is not related to any other anomaly, and partly because heredity is the governing cause. With deaf-mutism it is very different. It, too, may accumulate in single generations, being most frequent in brothers

and sisters and much less frequent in the older generations. In these, however, there can be found a comparatively large number of cases of partial or total deafness, insanity, epilepsy, retinitis pigmentosa, etc., which seems to indicate that deaf-mutism is, in many cases, a combined result of the transmission of various influences. These influences fall into two groups, those which originate in ear diseases, and those which originate in nervous disease in the family. Now, as the morbid anatomy of deaf-mutism proves that in the majority of cases the deafness causing deaf-mutism arises from abnormalities of the nervous parts of the auditory organ,—the labyrinth,—there is reason to suppose that in many cases deaf-mutism is caused by the transmission of the above dual influences through the parents. Supposing this hypothesis to be correct, our knowledge of the laws of heredity in deaf-mutism assumes at once a more distinct form, though we cannot ever expect it to be as clear as it is, for instance, in regard to the laws which govern hemophilia, for, as above mentioned, the causes of deaf-mutism are too numerous and varied. Even twins, who would seem to be exposed to exactly the same influences during fetal life, are sometimes the one a deaf-mute, the other a normal subject.

I may mention at last that, according to my opinion, the circumstance that insanity, epilepsy, retinitis pigmentosa, etc., are comparatively frequently found among the relatives of deaf-mutes points into that direction, that congenital deaf-mutism belongs to the degenerative phenomena of the human race.

In the absence of reliable statistics it is difficult to ascertain how far inheritance is likely to be intensified by the intermarriage of the deaf. Such marriages are not very common in

Europe. In the United States, however, where for the last half-century a great deal of attention has been paid to the education of the deaf, and where, consequently, they have been more intimately brought together, so much intermarriage has gone on as to excite the alarm of many observers. In 1884 Graham Bell, the well-known creator of the Volta Bureau of Washington, published his "Memoir upon the Formation of a Deaf Variety of the Human Race," and now Fay comes forward with an elaborate inquiry into the result of "Marriages of the Deaf in America." By means of circulars and other investigations, Fay has collected a total of 3078 marriages, sufficiently reported for conclusions to be drawn from them, and which he has reason to believe represent all the marriages of this kind which have taken place on the continent of North America within a given period. These results he has tabulated and analyzed, and, as far as the figures allow, he shows that the average of sterility is not greater among such marriages than among the general population; that marriages where both the parties are deaf do not intensify the chance of deafness being inherited by the children, but double it; that, since deafness is due to a variety of causes, parents are less likely to transmit their defects whose deafness is due to different causes, and that congenitally deaf parents are far more likely to transmit their deafness than are those who have become deaf since their birth. As to the effect of consanguineous marriages, they have no effect beyond the ordinary laws of inheritance—that is, the probability of inheritance by the children of the defects of their parents is not intensified by the relationship, but is proportionate to the amount of deafness in the ancestry. A. H. Huth (*Lancet*, Feb. 10, 1900).

The writer, while medical officer at the Indiana Institute for the Education of the Deaf, carefully studied 317 cases of deaf-mutism. Of these,

183 were boys and 134 girls. The average age was a little more than 12 years. The causes given by parents and family physicians were as follows: born deaf, 119; brain fever, 36; cerebrospinal meningitis, 34; catarrh, 20; otitis media, 16; scarlet fever, 15; traumatism, 11; influenza, 9; measles, 6; typhoid, 7; malaria, 11; scrofula, 4; whooping-cough, 3; mumps, 3; diphtheria, 2; pneumonia, 2; quinine, 2; earache, 1; inanition, 1; eczema, 1; unknown, 9; paralysis, 1; spasms, 1; tonsillitis, 1. J. G. Wishard (Ind. Med. Jour., Aug., 1903).

The writer examined 800 deaf-mutes with an autopsy in 154 cases. In about 68 per cent. of the entire number the condition was congenital; in the remaining 32 per cent. the deaf-mutism had been acquired in consequence of lesions in the auditory apparatus, including affections of the auditory centers in the cortex. The autopsy findings emphasize the importance in the etiology of the causal lesions in the labyrinth, cortex, or medulla, of meningitis, of infectious diseases, and of accidents involving the skull. Suppuration of the middle ear or of the Eustachian tubes has much less etiological importance. Castex (Bull. de l'Acad. de Méd. de Paris, vol. lxxix, No. 5, 1905).

Fifty per cent. of the cases are due to congenital causes and an equal number are acquired. Two facts in the congenital variety are noteworthy: heredity and consanguinity of parents. This would indicate that marriage among the deaf is to be discouraged. In acquired deaf-mutism brain diseases form the most important causative element, especially meningitis. Next in importance are the acute infectious diseases, especially scarlet fever, measles, and diphtheria. Constitutional diseases, especially syphilis, are occasionally responsible. Mackay (Practitioner, Oct., 1908).

Hysterical mutism is usually of sudden origin and the result of some severe psychical or emotional shock. It differs from hysterical aphonia in

that the former evinces a more extended disability of the mechanisms of speech, and it differs from aphemia or motor aphasia in that the mutism is absolute. The treatment may be either brusque in character or gentle and persuasive. An effort should always be made to "scare-back" the voice, and then by psychophysical training to re-establish correct methods of speech, but failing in this treatment, milder educational measures should be used, viz., suggestion, persuasion, and re-education. G. Hudson-Makuen (N. Y. Med. Jour., May 27, 1916)).

The deafmutes in Switzerland have never been accurately recorded, but the census of 1870 showed 24½ deaf-mutes to 10,000 inhabitants, while the average for the other European countries is scarcely 8. In the Bern district the figure was 42, in Lucerne 44, and in Wallis 49. The districts in which goiter and cretins are most numerous also seem to be endemic foci of deafmutism. Siebenmann (Correspondenzbl. f. Schweizer Aerzte, Jan. 5, 1918).

The writer's extensive investigation of deafmutism in the Malmö district revealed 383 deaf mutes, that is, about 8.4 per 10,000 inhabitants of that region. The proportion was 10.9 in the towns and only 6.8 in the rural districts. Only 28.2 per cent. of all were known to be congenitally deaf. In the district investigated, direct transmission of congenital deafmutism to the offspring does not seem to be much of a factor in deafmutism. On the other hand, deafmute marriages result in few offspring. Prohibition of consanguineous marriages would not accomplish much as the parties could get married in other countries or cohabit without marriage. The most important factor in deafmutism is seen by these researches to be infectious diseases, and it is against these that prophylactic measures should be directed. F. Bergh (Jour. Amer. Med. Assoc.; from Svenska Lakare. Handl., Dec. 31, 1918).

**Consanguinity.**—The question of the importance of consanguinity as a cause of deaf-mutism has been a fruitful subject of discussion. The first decidedly expressed opinion upon this topic appeared in 1846, when Ménière and Puy-bonnieux, who were, respectively, medical attendant and teacher at the State Deaf and Dumb Institution in Paris, laid great stress upon the important part which consanguinity played in deaf-mutism, without, however, producing statistics in support of their theory. Such, however, appeared shortly after in the returns of the Irish census of 1851, which was the first to include this question in its rubrics, and, from the results thus obtained, Wilde came to the conclusion that “among the predisposing causes of mutism the too-close consanguinity of parents may be looked upon as paramount.” Vulliet, Landes, Chazarain, Bemiss, Howe, Dahl, Boudin, Mitchell, and the undaunted defender of the doctrine of consanguinity, Devay, were all in favor of the importance of this factor in the etiology of deaf-mutism, while Bourgeois, Périer, Huth, Voisin, and G. Darwin were more or less opposed to the hypothesis that consanguineous marriages predispose to degeneration in the offspring, deaf-mutism being generally the principal object of their arguments. Statistical information as to the frequency of consanguinity among the parents of deaf-mutes has also been forthcoming, the frequency with which deaf-mutes are reported as being born in consanguineous marriages varying from 1.6 to 9.4 per cent., while the percentage for deaf-mutes with congenital deafness varies from 2.8 to 23.0 per cent.

It will be seen, then, that statements as to the frequency with which deaf-mutes are born in consanguineous mar-

riages differ considerably. This can most naturally be explained as resulting from various circumstances. To begin with, such marriages vary in frequency in different countries; thus, in Prussia they form only 0.8 per cent. of all marriages; in France, 1 to 2 per cent.; and in England, 3 to 4 per cent. at the outside; in Denmark, 3 to 4 per cent.; in Saxony, 4, and in Norway over 6.65 per cent. Further, there is no doubt that the frequency of consanguineous marriages differs in the different confessions and classes of society, in cities and in the country, and here, also, in different districts. It must also be observed that the various statistics sometimes embrace whole countries, sometimes single districts, and sometimes deaf-and-dumb institutions, clinics, etc. The information in question has also been obtained in different ways; for instance, by reports, censuses, individual investigations, etc., and finally the different authors have included different degrees of relationship.

Although many investigators have found comparatively few deaf-mutes born in consanguineous marriages, there are several circumstances which seem to prove that consanguinity is an important factor in the etiology of deaf-mutism. They are the following:—

Several statistical reports the reliability of which cannot be doubted are to the effect that deaf-mutes are comparatively often born of consanguineous marriages, and there seems to be reason to lay greater stress upon such positive results than upon those pointing in a negative direction.

All authors are unanimous in declaring consanguineous origin to be more common among congenital deaf-mutes than among deaf-mutes in general. This indicates that it is deaf-mutes with



acquired deafness who reduce the rate that expresses the frequency with which deaf-mutes in general are born in consanguineous marriages. That consanguinity plays a part in congenital deafness only, or almost only, may be seen from the circumstance that all authors who have occupied themselves with this subject have come to the result that deaf-mute children born of consanguineous marriages are, in the majority of cases, born deaf, while only a small majority become deaf after birth.

That consanguinity is of importance in the etiology of deaf-mutism is evident from the circumstance that several authors have proved that, among the marriages of which the deaf-mutes are born, the consanguineous unions produce a larger number of deaf-mutes than the crossed.

Finally, several statisticians have proved that the closer the degree of relationship between the parents, the larger was the number of deaf-mute children born.

It will be seen that there are various circumstances which clearly indicate that the intermarriage of relatives plays no insignificant part in the etiology of deaf-mutism. Everything, however, tends to prove that it is entirely, or principally, in congenital deafness that consanguinity is an important etiological factor.

It is, however, undecided whether consanguinity in itself is a remote cause of deaf-mutism, or whether it is through the intensified transmission of hereditary, morbid conditions or tendencies prevalent in a family that it makes itself felt. Theoretical considerations and a few lately published investigations in Norway by Uchermann are strongly in favor of the latter supposition; still, it is but fair to say that up to the present

there have not been many or convincing facts brought forward in its support.

There are, then, but few facts which serve to elucidate the question whether the influence of consanguinity upon deaf-mutism is direct or indirect. Further investigations of the same nature will, perhaps, throw more light upon this subject. The final solution of the question will, however, in all probability, only be brought about by means of information as to the family, supported by an exact knowledge of the relatives of the deaf-mutes, and supplemented by their thorough objective examination. It is only thus that it will be possible to find less pronounced, but not on that account less important abnormalities in the family, and to discover with what frequency the influence of heredity can be, with certainty, excluded in consanguineous marriages resulting in deaf-mute children.

There are, besides the above-mentioned, several other remote causes, which are, more or less properly, supposed to play a part in the etiology of deaf-mutism; of these the most important are the following:—

*Alcoholism in the Parents.*—Although the abuse of alcohol is extremely common, and although we have no information as to its frequency, on the whole, still, several reports seem to indicate that alcoholism in the parents plays some part in the etiology of deaf-mutism. Among the most important facts as to this question must be mentioned those stated by Uchermann in Norway, where, in cases of deaf-mutism of non-hereditary origin, alcoholism was found twice as often among the parents of the deaf-mutes with congenital deafness than among parents of deaf-mutes with acquired deafness. It is at present impossible to form any

accurate opinion as to whether alcoholism makes itself felt by weakening the parents' constitution, or whether it is an expression of a nervous disposition.

*Syphilis in the Parents.*—This disease has, on the whole, been found comparatively seldom among the parents of deaf-mutes. This does not, however, prove that syphilis plays no part in the etiology of deaf-mutism, for it is often difficult to discover, by questioning, whether a person has or has not had this disease, and it is also possible that investigations have, up to the present, been deficient in this particular. It is, at all events, certain that syphilis in the parents may produce a form of deafness in the children, appearing in the later years of childhood, and often leading to deaf-mutism. This form of deafness will be mentioned more particularly under the special etiology of acquired deaf-mutism.

*Age and Difference in Age of Parents.*—Ménière was the first to draw attention to these two factors in the origin of deaf-mutism, stating that, according to his experience, deaf-mutes were often the children of young parents, and that such marriages were frequently sterile or resulted in weakly offsprings. Later investigations have, however, not confirmed this.

*Fertility of Marriages.*—All authors who have directed their attention to this subject agree that marriages producing deaf-mutes are remarkable for their fertility. According to Uchermann, this may be explained by supposing that the greater number of children there are born, the more strongly the hereditary disposition to deaf-mutism, hemophilia, etc., shows itself.

(B) *Immediate Causes.*—According to recent statistics, in about one-half of the cases of acquired deaf-mutism the

deafness is acquired during the first three years of infancy, the greater number of cases falling in the third (statistics from the United States) or the second (European statistics) year of life; then comes the fourth, the first, the fifth, sixth, and so on.

*Brain Diseases.*—These play an important part in deafness acquired after birth and resulting in deaf-mutism. The Irish statistics of 1881 show the lowest figure, viz.: 11.9 per cent., and the Pomeranian report the highest, viz.: 54.5 per cent. It will be seen that the importance of brain diseases in the etiology of deaf-mutism varies considerably in the different countries; this is not only due to the circumstance that the expression "brain disease" includes different affections in the different reports, but also to the varying intensity with which cerebral disease appears at different times and at different places. All modern investigators agree, however, that brain diseases are at present the predominant cause of acquired deaf-mutism.

There can be no doubt that the most frequent brain disease leading to deaf-mutism is *epidemic cerebrospinal meningitis*, the deleterious influence of which has been especially pointed out by Moos. We possess various clinical observations of partial or complete deafness caused by epidemic cerebrospinal meningitis, and post-mortem examinations of persons whose deafness is due to this disease or other similar brain diseases, which elucidate the manner in which cerebral affections act deleteriously upon the infantile organs of hearing. The great conformity which exists between the changes in the auditory organs caused by cerebrospinal meningitis and changes declared to be due to inflammation of the brain in general, or

to other diseases with pronounced cerebral symptoms, authorizes us to suppose that the facts related in the following paragraphs hold good for the majority of cases of deaf-mutism caused by acute brain disease.

Clinical experience teaches us that the very considerable defects in hearing which appear during epidemic cerebrospinal meningitis may have a dual origin, viz.: inflammation of the middle ear or an affection of the labyrinth. Loss of hearing from the former cause is, however, exceedingly seldom so considerable or so lasting as to result in deaf-mutism. Deafness resulting from labyrinthine disease is more rare, but, at the same time, of more importance, since the loss of hearing is, as a rule, very considerable, often, indeed, total, generally affecting both sides and nearly always permanent. According to Moos and Knapp, labyrinthine deafness in epidemic cerebrospinal meningitis generally appears suddenly, seldom gradually. As a rule, it appears in the course of the first two weeks, but may also show itself later; Knapp reports a case where it appeared even six weeks after the commencement of the disease.

The pathogenesis of the labyrinthine disease from meningitis is always the spreading of the inflammation of the leptomeninges to the membranous labyrinth, causing here a suppuration which later is developing to the formation of granulations, connective tissue, etc., with total or partial destruction of the inner ear.

*Acute Infectious Diseases.*—The importance of this group of diseases in the etiology of deaf-mutism is doubtless at present less marked than that of brain diseases. If, however, epidemic cerebromeningitis is included among acute infectious diseases,—to which group it

doubtless belongs,—they immediately assume a very prominent place, and there can be no hesitation in declaring that the great majority of cases of deaf-mutism caused by acquired deafness are the result of acute infectious diseases. The importance of the parts played by the different diseases varies greatly, as will be seen, scarlet fever predominating.

Scarlet fever (scarlatina). This disease has always and in all countries been recognized as a very frequent cause of infantile deafness, and, consequently, of deaf-mutism. The influence of scarlet fever on deaf-mutism differs, however, in different countries and at different times, which is doubtless due to the varying intensity and character with which the disease appears. The lowest figures are represented by statistics from Italy (1.5 per cent.), the highest from Saxony (47.6 per cent.).

The origin of deafness in scarlet fever has been elucidated by clinical research, which proves that ear diseases caused by scarlet fever generally consist of inflammation of the middle ear, with a marked tendency to destroy the mucous membrane and osseous walls of the tympanum, and also the auditory ossicles. The inflammations of the middle ear, which are most frequently propagated through the Eustachian tubes, but which may, perhaps, appear independently, are not, as a rule, in themselves capable of causing a diminution of hearing in infancy so lasting and so considerable as to result in deaf-mutism, unless the labyrinth is affected. Scarlatinal deafness resulting in deaf-mutism is then, doubtless in most cases, due to a partial or entire destruction of the membranous contents of the cochlea. This destruction is, in most cases, caused by the propagation of the inflammation to

the internal ear through the fenestræ, and almost exclusively through the fenestra ovalis, leading from the tympanum to the labyrinth. In post-mortem examinations of deaf-mutes whose deafness was the result of scarlet fever, indications of an inflammation of the middle ear has also been found; also abnormalities in one or both fenestræ, doubtless the result of an inflammatory process. On the other hand, there are various circumstances which indicate that scarlatinal affections of the labyrinth may appear independently of an inflammation of the middle ear, or that, if such inflammation had existed, it has been very slight. Thus, for instance, it is often found, on otoscopic examination of deaf-mutes who have become deaf after scarlet fever, that the drumhead exhibits but slight or no abnormalities.

Measles (*morbilli*). The reports relating to the frequency of measles as a cause of deaf-mutism vary greatly, though not so much as was the case with scarlet fever, which disease also assumes a much more prominent rank in the etiology of deaf-mutism; the lowest rate is Württemberg and Baden (1.0 per cent.), the highest Mecklenburg-Schwerin (8.3 per cent.). The deafness caused by measles is always due to labyrinthine changes, which are, in the most cases, secondary to inflammation of the middle ear and rarely of hematogenic origin.

Among other infectious diseases which now and then cause deaf-mutism may be mentioned the different varieties of typhus (typhoid fever, exanthematic typhus), diphtheria, small-pox, chicken pox, erysipelas, dysentery, influenza, ague, whooping-cough, mumps, inflammation of the lungs, and rheumatic fever.

*Constitutional Diseases.*—Of these may be mentioned rickets, scrofula, and

syphilis. Although syphilis is represented in most statistics relating to the causes of deaf-mutism by only a fraction or not at all in modern statistics, there can be no doubt that when inherited from the parents it plays some part in deafness acquired in infancy and resulting in deaf-mutism. Inherited syphilis may, as is well known, produce a peculiar form of deafness accompanied by certain ocular affections, which, it is true, generally appears after the age of puberty, but which, however, also shows itself before that period, even as early as the age of 4. The circumstance, however, that hereditary syphilitic deafness often appears without any other marked symptoms of syphilis, and that it is extremely difficult to discover syphilis in the parents, especially by questions alone, explains why this disease is so seldom noticed in the parents of deaf-mutes in hitherto published statistics. It seems, also, that acquired syphilis may cause deaf-mutism; but no investigators have, up to the present, touched upon this subject.

*Injury (Trauma).*—Although it is probable that traumatic influences, such as falls, blows on the head, etc., to which children are especially subject, are sometimes stated as being the cause of deaf-mutism in cases of really congenital origin, there is no doubt that such causes may produce deafness resulting in mutism, as ear diseases of traumatic origin are not at all unknown, even among adults. Injury also is included in the causes of deaf-mutism in nearly all the more considerable statistics, the figures, however, being but small.

**MORBID ANATOMY.**—Although a partial examination of the auditory organs of deaf-mutes during lifetime is possible, still it can only embrace the peripheral parts, and there must always

be a difficulty in deciding whether the morbid changes thus revealed are of primary or secondary importance, or, indeed, only accidental. It is, therefore, only possible to arrive at an intimate knowledge of the morbid changes causing deaf-mutism, and, hence, at the just comprehension of its nature, by means of post-mortem examination. We have but few reports of such examinations dating earlier than the commencement of this century, and they yield so little information that we can only surmise that the examinations have been incomplete.

Before discussing the different parts of the auditory organs in which morbid changes have been found, it must be observed that several investigators have found no changes whatever in some of the cases examined by them; indeed, Ibsen's and Mackeprang's investigations gave negative results in no less than one-third of all their cases. As, however, these investigations date from a period when the microscopic examination of the labyrinth was but little developed, and as no mention is made of an examination of the brain or of the auditory nerve, the negative results arrived at lose considerably in importance, for it is impossible that the parts of the auditory organ above mentioned have been the seat of undetected abnormalities.

*Morbid Changes of the Middle Ear.*—If we take a survey of the pathological changes of the middle ear which have been found in post-mortem examination of deaf-mutes, we shall find that such changes are remarkably frequent. It is only exceptionally that these have been the result of malformation; they have, in the majority of cases, owed their presence to inflammatory processes or the remains of such. These inflammatory processes have sometimes been

of catarrhal nature, but generally suppurative, in which cases they have been intense and destructive. The abnormalities which are characteristic of the morbid anatomy of deaf-mutism have comparatively frequently had their seat about the two fenestræ, especially in and around the fenestra rotunda, which, in several cases, has been found closed by osseous masses. In the majority of cases, however, the abnormalities of the middle ear have been accompanied by marked changes of the inner ear.

Cases of deaf-mutism with no labyrinthine anomalies are, on the whole, to be considered with great suspicion, as it is likely that they have been incompletely examined.

*Macroscopic Morbid Changes of the Labyrinth.*—These have affected either the whole labyrinth or only parts of it. The so-called entire absence of the labyrinth plays an important part among the former class, partly on account of its comparative frequency, and partly on account of its origin. The majority of authors have hitherto regarded the absence of the labyrinth as the result of arrested development. I have, however, in several of my works proved that partial or complete absence of the labyrinth, or parts of it, may be, and probably frequently is, caused by the deposit of osseous tissue in the labyrinthine cavity, which becomes thus more or less completely filled up, under which process the normal outlines may disappear entirely. Such a formation of osseous tissue is, without doubt, the result of a previous inflammatory process; that is, of an *otitis intima*. I have also pointed out that it is often impossible to distinguish between fetal and postfetal morbid changes by post-mortem examination, unless accompanied by exhaustive and reliable information as to the cause

and date of the affection. From the following it will be evident that the deposit of osseous tissue in the cavity of the labyrinth is one of the most frequent labyrinthine anomalies found upon post-mortem examination of deaf-mutes, the osseous mass sometimes filling the whole cavity, while sometimes only a section exhibits a parietal deposit which has merely caused a diminution of the cavity in question. The most extensive formations of osseous tissue in the labyrinth are apparently the result of a postnatal *otitis intima*. It is interesting to observe that various investigators have discovered such osseous deposit sometimes on the one side only, sometimes on both, some having also found osseous tissue on the one side, and deposits of chalk or fibrous tissue—which may also, as is well known, be the result of inflammatory processes—on the other side, while both the latter deposits have also been frequently found in the labyrinths of deaf-mutes when there was no formation of osseous tissue on either side. Inflammatory and also degenerative processes may leave other products behind them, which may appear in like manner in other parts of the body. I would not, however, imply that the partial or total absence of the labyrinth may not be the result of arrested development, which, on the other hand, may be due to fetal inflammatory processes. Still, it is often difficult to find proofs that such has been the origin of the abnormalities in individual cases. In many cases the inflammatory process in the labyrinth causing its partial or complete destruction was secondary to an inflammation of the middle ear. According to the reports of several post-mortem examinations, the inflammation of the middle ear was due to acute infectious diseases, in particular scarlet

fever and measles. In conformity with the above it will be seen that in dissections in which the complete or partial absence of the labyrinth was discovered tolerably well marked changes were found in the middle ear, consisting, in great part, in the remains of inflammatory processes, and this was true of many of the cases which will be mentioned farther on as examples of circumscribed deposit of osseous substance in the labyrinth. On the other hand, the absence of inflammatory processes in the middle ear, or the traces of such, and in other cases the histories of the cases seem to indicate that the labyrinthine inflammation is not of necessity propagated from the middle ear, but that it frequently originates in the membranes of the brain. This is especially probable in all cases where meningitis is with certainty stated to be the cause of deafness. There is, perhaps, a third kind of labyrinthine inflammation—viz., primary inflammation—which has been especially defended by Voltolini and called after him *otitis intima* of Voltolini. The existence of this affection cannot be proved or disproved by arguments drawn from the material here under discussion. Besides the macroscopic morbid changes of the labyrinth described above as being of postnatal or of congenital inflammatory origin, there are a small group of cases reported in literature as cases of undoubted *congenital malformations* of the labyrinth, of which, however, some also might be caused by intra-uterine inflammatory processes. One of the most interesting of these cases was that observed by Michel, in which the mastoid process and the entire osseous labyrinth were wanting, the petrous bone being quite deformed. In one group of cases, described by Liebermann, in his exhaust-

ive work on the anatomy of deaf-mutism, as "the type Mondini," the vestibular aqueduct is enlarged and the top of the cochlea is flattened, consisting only of one large cavity, in which the modiolus, the spiral lamina, etc., are wanting.

As far as the seat of the labyrinthine changes in deaf-mutes is concerned, the vestibule (with the exception of its aqueduct) is the part of the labyrinth which has been least frequently found to be the seat of morbid changes. The reason is that the vestibule is, comparatively speaking, seldom found to be abnormally changed on post-mortem examination of deafborn deaf-mutes, anomalies in the two other principal sections of the labyrinth being twice as frequent in these cases. It is also remarkable that in no hitherto-published post-mortem examination of a deaf-mute with acquired or congenital deafness, or where the origin of the deafness is not stated, has the vestibule been the only section of the labyrinth which has been the seat of abnormalities, the other sections being also changed when this has been the case with the vestibule.

The semicircular canals are decidedly the portion of the labyrinth which is most frequently the seat of pathological changes; these are, indeed, so frequent here that more than one-half of the dissections have yielded positive results. Indubitable cases of congenital malformations have been observed by several investigators, but it is questionable whether such abnormalities as the union of the two canals into one, shortening or lengthening of the canals, etc., are to be regarded as of vital importance. In not less than one-fifth of all the dissections yielding positive result the semicircular canals were the only part of the labyrinth which exhibited morbid changes.

In the majority of cases in which the semicircular canals have been the seat of abnormalities they, or a part of them, have been filled up by osseous tissues, or must have been supposed to have been so; for instance, in many cases where the reports simply mention "absence" of these canals. The posterior canal has been most frequently attacked, either above or together with the superior, but principally together with both the superior and the external. There is no reason to presume the frequent occurrence of abnormalities of the semicircular canals to be a frequent cause of deaf-mutism, but only a conspicuous proof of the frequency with which labyrinthine inflammations are a cause of that anomaly, for, of course, destruction of the membranous part of the semicircular canals alone does not produce deafness. This symptom is only produced by total, or almost total, destruction of the contents of the cochlea or of the auditory nerve, while destruction of the contents of the semicircular canals and the vestibule results in suspension of the static function of the labyrinth. Disturbances of the equilibrium are, therefore, very common in deaf-mutes, as proved by several investigators.

Morbid changes of the cochlea are somewhat more frequent than those of the vestibule, and are very equally divided between congenital and acquired cases of deaf-mutism. In several cases the cochlea was the only part of the labyrinth which was the seat of morbid changes; in the great majority of cases, however, other parts of the inner ear have been abnormal, the semicircular canals having been at the same time especially frequently the seat of anomalies. The more or less entire filling up by osseous or calcareous masses is the

anomaly most common to the cochlea, and under this heading may doubtless be included all cases in which the cochlea is reported to be entirely absent, or in which only one or two cavities remained. Abnormalities of this nature are mentioned in about one-eighth of all hitherto-published post-mortem examinations.

Unchermann found in 1885 about 1841 deaf-mutes in Norway, of whom 51 per cent. were due to heredity, and the remaining per cent. acquired, with the exception of 0.5 per cent., in whom it could not be determined. It is not always possible to determine, even by examination after death. Most cases of acquired deaf-mutism are caused by diseases of the labyrinth, most of which have spread from the brain or middle ear. Mygind, in his work in 1894, reported over 139 cases in which the middle ear only was diseased, but he stated nothing about the labyrinth or the histological examination of the labyrinth. Thus Matte could completely deny the occurrence of deaf-mutism due solely to middle-ear disease. Two personal cases in which the middle ear only was demonstrable as a cause of the deaf-mutism. J. Habermann (*Archiv f. Ohrenh.*, Bd. liii, S. 52-67, 1901).

The writer, having had opportunity to examine the petrous portion of the temporal bone in a young woman who had been a deaf-mute from infancy, found that, while the external and middle ears were normal, both labyrinths showed anomalies evidently of embryonal origin: atrophy of the spiral ganglion, cochlear nerve, and remus sacularis, with entire absence of the papilla basilaris on both sides, and with marked aplasia of the Corti organ. These and other findings were similar to those of 10 similar cases that he had examined histologically. Lindt (*Deut. Archiv f. klin. Med.*, Bd. lxxxvi, Nu. 1-3, 1906).

**Microscopic Morbid Changes of the Labyrinth.**—In many cases of post-

mortem examinations of deaf-mutes in which the labyrinth was found to be without macroscopic changes, there is

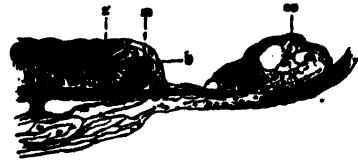


Fig. 1.

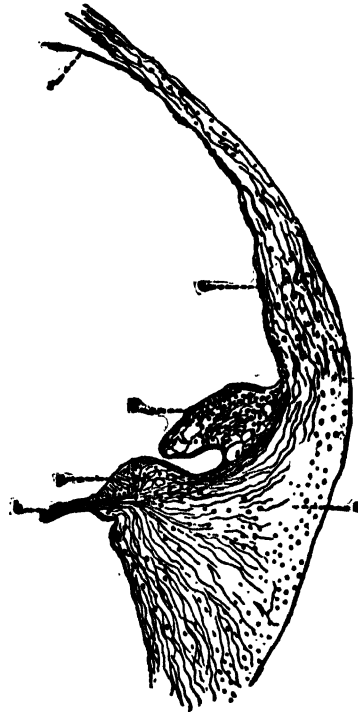


Fig. 2.

Auditory atrophy and anomalies of development in the membranous labyrinth of both ears in a case of deaf-mutism. (Scheibe.)

Fig. 1.—*f*, Corti's organ; *z*, increased cells in the sulcus spiralis; *b*, arched layer of cells, extending to the limbus laminae spiralis osseae; *m*, Corti's membrane.

Fig. 2.—*s*, stratum semilunare; *b*, beginning of basilar membrane; *p*, prominentia spiralis; *l*, ridge on the stria vascularis; *e*, flat cells on the rest of the stria; *r*, a piece of Reissner's membrane, bulged forward toward the scala vestibuli; inserted somewhat peripherally, and extending farther on, in a thicker layer of cells. (*Zeitschrift für Ohrenheilkunde*.)

no mistake that the deafness has been caused by microscopic changes of the membranous part, which either have not been looked for or which have been overlooked. Liebermann describes the



microscopic changes of the labyrinth found in deaf-mutes with congenital deafness under the following heads: (1) cases of degeneration of the epithelium of the lamina spiralis membranacea of the cochlea; (2) cases of degeneration of the epithelium of the whole

324) can be mentioned, the details of which are seen by Figs. 1 to 4.

*Morbid Changes of the Auditory Nerve.*—It is a fact that, although atrophy and degeneration of the auditory nerve, or a part of it, are frequent in deaf-mutes, they are far from being

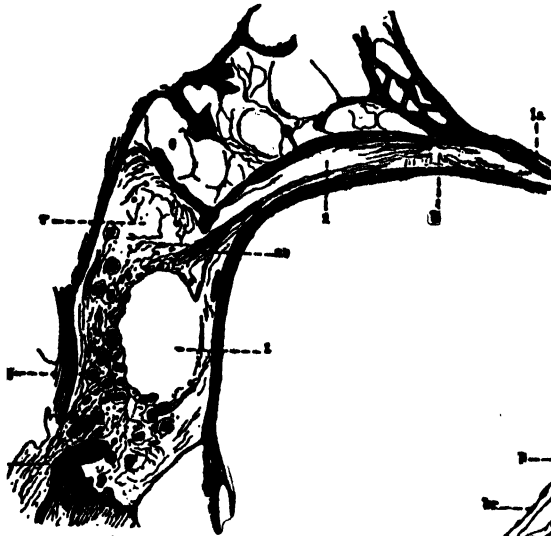


Fig. 3.

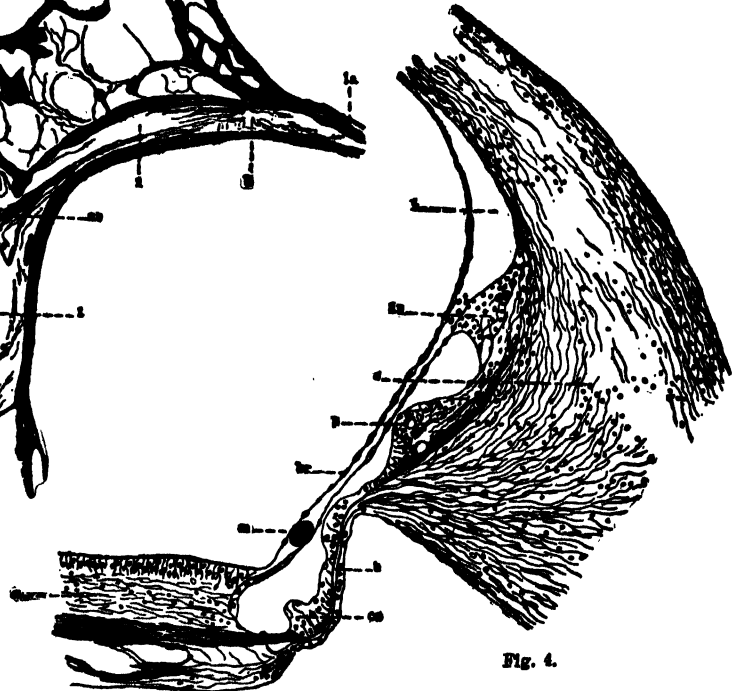


Fig. 4.

Auditory atrophy and anomalies of development in the membranous labyrinth of both ears in a case of deaf-mutism. (Scheibe.)

Fig. 3.—*r*, Rosenthal's canal; *la*, lamina spiralis ossea; *g*, ganglion-cells; *l*, lacuna; *n1*, entering nerve-fibers; *n2*, departing nerve-fibers; *b*, connective tissue.

Fig. 4.—*s*, semilunar stratum; *c*, crista spiralis; *b*, basilar membrane; *co*, Corti's organ badly preserved; *p*, prominentia spiralis; *br*, bridge; *l*, lacuna in the stria vascularis; *ls*, ridge with attachment to the lower part of the bridge; *m*, rudimentary Corti-membrane. (Zeltchrift für Ohrenheilkunde.)

ductus cochlearis, spreading generally also to the sacculus, while aqueductus vestibuli and the saccus endolymphaticus are rarely, and the utriculus and the ampullæ still more rarely, attacked; the second form is generally combined with ectasia and collapse of membranous wall. As a typical example of the latter form, the case described by Scheibe (Arch. of Otology, vol. xxiv, 1897, No.

always present, as believed by many, since Hyrtl put forward that supposition, based upon post-mortem examinations performed by him. As it is to be supposed that the auditory nerve of the majority of deaf-mutes examined *post mortem* has been out of function some time, without there being found any atrophy or degeneration in it or its branches, it would seem that this nerve

is not particularly disposed to become atrophied or degenerated from inactivity. The correctness of this hypothesis is confirmed by morbid anatomical examinations hitherto published of persons who have become deaf at a more advanced age, which examinations all point in the same direction. The cases of atrophy or degeneration of the auditory nerve which have been found by post-mortem examinations of deaf-mutes seem, therefore, as a rule, to be due to some other cause, and we are obliged to regard them as the result of either congenital malformations of this nerve or of postnatal inflammatory processes of it, or centripetal atrophy or degeneration subsequent to labyrinthine destructive processes, or as the expression of a centrifugal change arising from primary disease of the central nervous system.

It is impossible as yet to give any satisfactory reason why the auditory nerve in some deaf-mutes is atrophied or degenerated while in others it is not. The question will doubtless be cleared up by a larger number of post-mortem examinations of deaf-mutes, accompanied by reliable information as to the origin of the deafness.

*Morbid Changes of the Brain (Cerebrum).*—The defective development of the surface of the third convolution and of the insula Reilii of the left side may be mentioned as an abnormality several times discovered in deaf-mutes, but which has no casual relation to deafness. Rüdinger and Waldschmidt found this abnormality in several deaf-mutes who presented no history of disease, and whose labyrinths were not examined, while other investigators found it in two deaf-mutes who had both become deaf after birth, in the third year, after meningitis and scarlet fever, respectively,

and who both exhibited pronounced abnormalities in the ear. The flattening of the cerebral convolutions is doubtless due to atrophy, caused by the inactivity of the parts of the brain which are known to be the motor center of speech, on account of the inactivity of the muscles of speech. In the two latter cases, also, there was information proving that the deaf-mutes in question had never learned to speak.

If we cast a retrospective glance over the foregoing facts it will be seen, first, with regard to the nature of the morbid changes met with in the hearing organs of deaf-mutes, that they do not differ, so far as their quality is concerned, from those generally found in ear diseases, but that the difference must be rather sought in the intensity and extent of the morbid processes. The abnormalities found in deaf-mutes may, at least in a great number of cases, be most naturally interpreted as being the results of intense and widespread inflammatory processes. This is particularly evident in cases referring to deaf-mutes who had become deaf after birth. It will further be seen that the abnormalities found in cases of congenital and acquired deafness often present exactly the same appearance; so that in many cases it is impossible to decide, from the post-mortem examination alone, whether the changes are of fetal or postfetal origin. It is thus evident that the formerly accepted opinion that deaf-mutism arising from congenital deafness was always due to congenital malformations of the auditory organs has not been confirmed, since abnormalities which are the indubitable expression of such malformations are not frequent. It must, however, not be overlooked that many cases of congenital deaf-mutism with negative result of the

post-mortem examination where no microscopic examination has been performed might have been caused by congenital microscopic morbid changes of the membranaceous labyrinth. The latter years have also brought forward some cases of congenital microscopic malformation of the contents of the cochlea, the details of which will be found in the book of Liebermann, referred to above. So far as the seat of the abnormalities was concerned, it was found that these were, as a rule, bilateral, but have often differed greatly on either side, both as to character and localization, and especially as to intensity. The few cases in which the principal abnormalities were confined to the one side, while the other was normal or only the seat of unimportant anomalies, must, for the present at least, be looked upon with suspicion. Finally, it has been proved that the middle ear has very frequently been the seat of changes, accompanied, as a rule, by important abnormalities in the inner ear. These were most frequently situated in the semicircular canals, least frequently in the vestibulum, but were only to be considered as the principal cause of deafness when they were seated in the auditory part of the labyrinth, the cochlea. The auditory nerve in many cases exhibited signs of atrophy and degeneration and a few other abnormalities, while in a considerable number of cases no changes were visible. In some few cases the brain deviated somewhat from the normal.

Deaf-mutism is, therefore, from an anatomical point of view, in most cases to be considered as a result of an abnormality of the labyrinth.

**PROGNOSIS.**—There is no doubt that the prognosis of the deafness which is the cause of deaf-mutism is highly

unfavorable; still, there exist some well-authenticated cases of deaf-mutes whose power of hearing has been at least partially restored.

**TREATMENT.**—It is as yet difficult to say in what cases treatment is indicated, as we have not reached farther than to the first experiments in that direction. I have for years endeavored to act according to the following rules when deaf-mutes have been brought to me for treatment: Treatment is most decidedly indicated when the deaf-mute suffers from suppurative inflammatory processes of the middle ear. Treatment can, at least in such cases, remove or diminish the danger which always attaches to suppuration of the middle ear. Uchermann's experience also proves that the defects in the power of hearing may be diminished in cases of this nature. On the whole, **treatment of any aural or nasal disorder** that may be present is always indicated.

Many deaf-mutes are not absolutely deaf. Of the 139 studied by the writer, the cause of deaf-mutism in one-half of the cases was congenital; 26 per cent. showed chronic rhinitis, 11 per cent. adenoids. Pathological changes in the middle ear were frequent, especially in cases of acquired deaf-mutism. Deaf-mutes who can hear must be separated from those who cannot, for they require and profit by practice in watching other people talk. All cases with otorrhea or nasal disease should be energetically treated to improve what hearing may remain. Rundström (Nordiskt med. Arkiv, Afd. 1, No. 3, 1901).

Treatment is also indicated in cases in which there are some traces of the power of hearing, and especially when this power exists with varying intensity, and where there are also symptoms of catarrhal conditions in the

middle ear (catarrhal changes of the membrana tympani, retraction of the manubrium of the malleus, occlusion of the tubæ, etc.); also catarrh of the mucous membranes adjacent to the ear, especially when there also exist hypertrophy of the adenoid tissue in the nasopharyngeal cavity.

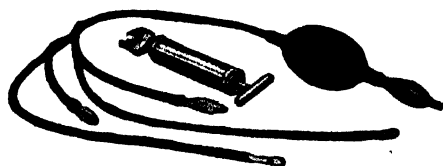
Case of acquired deaf-mutism, probably due to impacted cerumen in the ear, in a girl who at the age of 3 had appeared to be deaf and to lose the power of uttering intelligible sounds. Nothing in the history pointed to any antecedent inflammation in the ears. Examination showed only **impacted cerumen**, which was **syringed out**. The ear was then **politized**. The drum membranes were found to be contracted and opaque, but otherwise healthy. Almost immediately the child began to show an appreciation of sounds and very shortly to resume its speech. Recovery was soon complete. Mayo Collier (*Med. Press and Circular*, Jan. 15, 1902).

Deaf-mutism by obstruction of the Eustachian tubes, when it is not due to actual destructive labyrinthitis, is probably due to fixation of the stapes in the oval window by inward-acting pressure on the tympanic membrane. This amounts to a dislocation of the stapes; the stapedius muscle, being subjected to extreme tension, becomes paralyzed and the result is deafness, which, occurring in young children, causes deaf-mutism. The reason why we have not been giving hearing to such deaf-mutes heretofore is that we could not pull the stapes outward and thus reduce the dislocation. Neither inflation nor suction with Politzer's bag will effect this reduction, nor will pulling or punching the tympanic membrane be of any avail.

We have long needed some artificial device to act as a substitute for the prostrated stapedius to pull the stapes back to its proper position. It has been repeatedly demonstrated that just as soon as the stapes is set

in proper position a deaf-mute will hear. The stapedius will regain its power and the hearing will remain unless the tubes are again occluded and the stapedius prostrated. This applies alike to congenital and the acquired deaf-mutism.

The writer has devised an **instrument** which will **raise the stapes** and give hearing to such deaf-mute patients as have not had the stapes bound too strongly by the results of inflammatory processes, and he has obtained good results, a number of cases having retained both hearing and speech. After hearing is established the use of words has to be acquired, and this usually necessitates persistent teaching. M. M. Stapler (*Jour. Amer. Med. Assoc.*, Feb. 6, 1909).



Suction instrument for reducing dislocations of the ossicular chain in deaf-mutes. (Stapler.)  
New York Medical Journal.

The writer emphasizes the necessity for training every bit of hearing which a child may possess, repeating the **exercises** again and again during the day and with different voices. He also urges the importance of commencing early, even at the age of 2, never letting the fourth year pass without commencing training. Fröschels (*Med. Klinik*, Feb. 15, 1914).

The various steps in the **re-education** of men who have lost the power of speech under emotional stress are given by the writer. They begin with rhythmic exercises in breathing, then in blowing out the light of a match, or a candle, then in blowing soap bubbles. The next step is to whistle, first one note, leading up slowly to whistling some very simple familiar tune. Then the vowels in turn, expatiating amply on the progress realized, but leaving actual speech to be casually rearoused spon-

taneously. Briand (*Progrès Méd.*, Sept. 5, 1916).

In the event of craniotympanic conduction still existing, the chances in this group of cases seem more favorable still. In cases of catarrh of the middle ear and adjacent mucous membranes, where no signs of hearing can be discovered after repeated examination, I have also attempted treatment, but my experience has not been favorable in this group of cases.

To all the above-mentioned groups the indications are the same, whether the deafness is congenital or acquired. Various circumstances, which have been pointed out in the foregoing pages, indicate that total deafness resulting from acute infectious diseases, especially cerebrospinal meningitis and scarlet fever, and accompanied by slight catarrhal changes, is due to a constant labyrinthine disease which defies all treatment.

So far as the nature of an ultimate treatment is concerned, it must be observed that general and special otological principles must be used as guides, and the treatment, in the majority of cases, should be local.

Treatment in other than the above-mentioned cases of deaf-mutism is, of course, justified when it is not accompanied by any danger to the patient, when it is indicated by otological principles, and when it is certain that the anatomical cause of the deafness is not situated in the brain. It is for the future to show what chance of improvement such cases have.

Urbantschisch's treatment is also worthy of mention. It consists in **regular acoustic exercises**, intended either to awaken or improve the power of hearing in deaf-mutes, and there is every reason to look forward to more exhaustive information as to

the results of such treatment with considerable interest.

**Systematic hearing exercises** are important features of the treatment.

As early as possible the writer endeavors to ascertain whether the patient is capable of receiving any ordinary impression. This is accomplished by using the loud and harsh tones of an accordion near the child. If it shows signs of fright, it can be assumed that there is auditory perception; if not, the effort is again made at the end of six months. In children from 3 to 4 years of age an object is shown to the child and its name shouted into the ear. With deaf-mutes who have been taught to speak and read, the exercises are begun by shouting a long-drawn-out vowel sound into the ear, at the same time pointing to the printed character. This is soon followed by the use of words of one syllable, and a child can thus be taught a vocabulary before he can distinguish clearly between the sounds of individual letters. The perception of a sound is not only due to its loudness, but also to its duration; therefore the words should be lengthened as much as possible. When the hearing is much reduced, this exercise requires an enormous amount of time and patience, and can only be carried out by individual instruction. The amount of effort required on the part of the patient is very great, and auditory fatigue appears early. As soon as this shows itself the exercise should be suspended.

Systematic hearing exercises not only develop the sense of hearing, but also the nervous pathway for auditory perception. It is a matter of experience that many deaf-mutes receive many auditory impressions which they are unable to interpret. Not infrequently persons are met with who are said to be unable to hear spoken words, but who on careful examination show an astonishing degree of hearing power. Of necessity, the method is only applicable to those deaf-mutes who have a perception of

sound. Unless this is carefully looked for it may never be known; when found, it may often be developed so that the patient can hear vowels, then words, and even short phrases. The extent to which the hearing power may be developed can only be determined by actual trial in a given case. V. Urbantschitsch (*Jour. of Eye, Ear, and Throat Dis.*, July-Aug., 1900).

The following **exercises** are typical of those used in the best schools for deaf-mutes: **Breathing** through the nose and mouth is first taught. The teacher breathes through the nose on a slate or a mirror and shows the two moist spots; the child learns to imitate this. The mouth breathing produces one spot. The low position of the tongue is necessary for proper speech. It is taught by showing the position and using the mirror, and by a breath exercise. This latter rests upon the fact that the child cannot produce a good-sized spot on the slate unless he keeps his tongue down. **Tongue gymnastics** are next used to limber up and train the muscles which have never received the proper development. The tongue is protruded, retracted, moved to each side, turned up, etc. Tongue training preparatory to various consonant sounds is introduced. **Vibration of the vocal cords** is taught by feeling. The pupil puts his hand on the teacher's chest and also on his own. He thus learns to make a tone. He learns to raise and lower the voice, and by careful drill is able to make a fairly good tone. The physiological alphabet consists of a set of diagrams giving the typical positions of the tongue and lips for the chief sounds of the language. Combinations of consonants and vowels are now read at sight. Through these combinations words and sentences are developed. **Lip reading** of words and sentences is taught by having the patient watch the teacher's lips while she distinctly enunciates some word. Thus he learns to pick up objects off a table, to point out parts of the body, to obey commands, etc. When deaf-

ness is acquired after the person has learned to speak, the teaching of lip reading should begin at once. The voice then retains its natural character and the person can go right along with his education. *Scripture (Med. Record, July 23, 1910).*

The oral systems are supplanting the sign system, there being now scarcely an institute where the latter is taught. The oral system allows its pupils to hold intercourse with every one, instead of only with other deaf mutes. Further, the sign and manual language is purely artificial, while the oral system attempts the restoration of normal speech. It tries to take advantage of the remnant of hearing which many deaf and dumb possess. N. J. P. Van Baggen (*Med. Rec.*, May 23, 1914).

My own remarks on the treatment of deaf-mutism have exclusively dealt with the deafness from which the mutism results. I will not go farther into the treatment of mutism by special methods of instruction, because this subject is not included in the aim of this article, which is prepared for those who are to give their attention to the diseases involved.

It will then be seen that, when a child is proved to have such deficient power of hearing that mutism is the result, removal of that deaf-mutism by treatment can only be hoped for in very exceptional cases. Therefore, there is still greater reason for considering the question of the prevention of deaf-mutism. The principal method of obtaining this object must be to submit all children who suffer from deafness which threatens to cause, or has caused, deaf-mutism to a rational examination of the ears and of the adjacent mucous membranes, and eventually to make the existing disease the subject of rational treatment.

Histological studies of the auditory and phonatory tracts have revealed

the morbid anatomy of deaf-mutism, but they have failed to point the way toward any definite conclusions with reference to the etiology of the affection and to its treatment. They do not enable one to distinguish even between so-called congenital and acquired deaf-mutism, and there is very little to be found in the pathological processes themselves which is suggestive of the particular disease or diseases which caused them. Inasmuch as the physiology of hearing is still a subject for discussion, it is not surprising that the pathology of deaf-mutism should be obscure and unsatisfactory. Deaf-mutism is not a disease, but is a result of a disease, the disease itself having long since run its devastating course and left behind the morbid processes upon which the final result, deaf-mutism, depends. Although these morbid processes are plainly visible in post-mortem examinations, they have in themselves no features sufficiently distinctive to enable one to draw any satisfactory conclusions. One cannot always be sure that they are not purely accidental anomalies or merely unimportant variations, and until they are compared and correlated with histological studies of normal auditory and phonatory tracts, and with previous clinical histories of the subjects examined, their value must ever remain exceedingly limited. Future progress in this line of work will come from a closer study of the diseases which are responsible for the morbid anatomy of deaf-mutism, rather than from a further study of the morbid conditions themselves. G. Hudson Makuen (N. Y. Med. Jour., June 8, 1912).

HOLGER MYGIND,  
Copenhagen.

**DEATH TESTS.**—The importance of such tests need hardly be emphasized. The two tests that are especially useful, according to an editorial (*La Clinica Medica Ital.*, Mar., 1915) first: A drop of ether is instilled into the conjunctival sac of 1 eye, the other being used as control. Reddening of the conjunctiva affords proof

that life still exists. The second, d'Hal-luin's, consists in passing a stylet to the heart through a small incision in 1 of the intercostal spaces. Any movement in the heart is communicated to the stylet. This may induce cardiac activity by gentle movements of the stylet, combined with artificial respiration.

D. Massana (Rev. de Med. y Cir. Pract., Sept. 21, 1916) gives an infallible sign of death introduced by Lecha Marzo, of Granada. It consists of an acid reaction of the tears, blood, and organs coming on immediately after death and may be readily tried by introducing a piece of blue litmus paper under the eyelid.

From observations made on 180 dead and 2000 living subjects the writer finds that the Lecha Marzo test is a certain sign of real death; that it is never found in life; that it is not constantly present; that it occurs usually from 1½ to 7½ hours after death; and that low atmospheric temperature may impair its action. R. Alvarez de Toledo y Valero (*La Cronica Medica*, Lima, Jan., 1918).

The writer reiterates that in countless healthy persons and in 1079 persons of both sexes and in many hundreds of cases of diseases of the eye (which he lists separately) the reaction of the tears during life was invariably alkaline. Tested after death, by slipping a scrap of litmus paper under the eyelid, the reaction equally invariably veered to acid. The change was sometimes evident in half an hour, and only exceptionally took up to several hours. Lecha-Marzo (*Plus Ultra*, Nov., 1918).

According to Zsako (*Munch. med. Woch.*, Jan. 18, 1916), tapping with the hammer on certain muscles elicits a reflex contraction up to from 90 to 240 minutes after death. The contraction can be elicited in the same way on the living, but it is more pronounced in the cadaver as there is no antagonistic tonus.

Terson (*Arch. d'Ophthal.*, June, 1917) states that the pupils respond slowly to light, as also to atropin and physostigmin for several hours after death; electricity sometimes contracts the pupil 5 or 6

hours after death. But cauterization, scraping, sulphate of copper and subconjunctival saline injections produce no redness in the still warm body 2 hours after supposed death. Instillations of ether may cause damage; the writer prefers dionin, which is followed by no reaction if applied 2 hours after death.

Satre (*Presse méd.*, May 9, 1918) recommends Icard's forcipressure method, based on the permanence or evanescence of the ischemia of the tissues induced by compression; also Lorain's old procedure of exposing the forearm, calf, or thigh to a flame; if the blister which forms is filled with air and bursts with a cracking noise leaving the dermis dry, the man is dead, whereas if the blister contains fluid, death is but apparent.

Icard (*Presse méd.*, Aug. 8, 1918) points out that in the fluorescein test the coloration of the eye is a feature of only accessory importance. The main indication is the golden yellow or orange coloration of the skin and mucous membranes. This sign becomes manifest even from the use of a minimal amount of fluorescein. Restoration of the circulation cannot fail to attract attention, the peculiar color of the skin revealing the condition at once. S.

**DELIRIUM TREMENS.** See ALCOHOLISM.

**DEMENTIA PRECOX.**—In the modern classifications of insanity dementia precox occupies a most prominent place, embracing a large group of cases which include several more or less different types of mental disease. These types have in common, however, certain important characteristics, viz., the occurrence early in life of a pronounced tendency toward the development of mental deterioration or dementia accompanied by various symptoms of fundamental similarity. The term dementia precox has come into general use only within the last decade, but was suggested as early as 1886 by Schüle to designate a group of cases of early

acute dementia. More recently, under the influence of Kraepelin, it has come to include other groups of cases which had previously been recognized and described, but considered as separate and distinct forms of insanity. Many of the cases formerly classified under paranoia, the catatonics described by Kahlbaum in 1869, and the hebephrenics by Hecker in 1871, upon critical observation over an extended period of time have been found to conform sufficiently in incidence, course, and symptomatology to justify classifying them all under the general term of "dementia precox." Thus we have three principal forms or types of the disease, the hebephrenic, the catatonic, and the paranoid, which present fundamental similarities, but in which the symptoms vary in their appearance, course, and prominence.

In point of numbers dementia precox is one of the most common forms of insanity, comprising, according to various estimates, from 20 to 25 per cent. of all admissions to institutions for the insane.

It has long been known that dementia precox patients constitute a large part of the chronic cases in the New York State hospitals for the insane, but it was something of a shock to learn when the first census of the psychoses of the patients resident in the civil State hospitals was taken on July 1, 1916, that of the total patient population of 35,213, 18,940, or 53.81 per cent., were cases of dementia precox. The census taken a year later showed that these cases had increased to 19,544; the percentage, however, had remained practically the same. The total number of dementia precox cases under treatment during the year was 21,070.

Kirby and Bleuler have called attention to the fact that certain dementia precox cases develop without



hallucinations or pronounced trends of any sort, and on account of the absence of psychotic symptoms, rarely reach the State hospitals, but become chronic loafers, beggars, tramps and poorhouse inmates. H. M. Pollock (*Dementia Precox Studies*, July 1, 1918).

In most cases the onset occurs between the ages of 15 and 30 years. The age limits are not well defined, and cases which cannot be differentiated clinically from dementia precox occur as late as 60 years, and, at the other extreme, in early childhood. The different forms vary considerably in age incidence, the hebephrenic occurring, as a rule, at an early age, the catatonic at a more advanced period, and the paranoid still later in life.

The term "dementia precox" should be carefully restricted to those cases in which mental deterioration at an early stage of the disease is clearly recognizable and should be carefully considered and if possible avoided in those cases in which a dementia may possibly be developed. R. Sachs (*Jour. of Nerv. and Mental Dis.*, June, 1905).

**SYMPTOMATOLOGY AND PSYCHOPATHOLOGY.** — In the different forms of dementia precox are met variations in the appearance, prominence, and grouping of the symptoms, in the progress of the disease, in the age incidence, the occurrence of remissions or recovery, and other factors which will be discussed under the different headings. But as all of the types exhibit certain characteristics in common, a general consideration of the psychopathology of dementia precox may not be out of place here.

The most fundamental and constant phenomenon of dementia precox is mental deterioration, or dementia. This is often of slow development, and it may be difficult to determine in

the early cases, but systematic search will usually reveal some mental deficiency. Frequent changes in positions of employment, incapacity for continued effort or for constructive mental work, are significant where the history is obtainable. In judging whether or not the mental inefficiency of a given case is due to deterioration it is necessary to know that individual's normal standard of mentality and education, as it is obvious that a low grade of intelligence is not necessarily a stage of deterioration, and deterioration is the keynote of dementia precox. The degree of dementia varies in the different cases from a slight mental impairment in some to the extreme poverty of the intellect simulating idiocy in others. Remissions are not uncommon in the course of the disease, and all of the active symptoms may disappear temporarily or even permanently; but a definite dementia once established is never replaced by a normally active, intelligent, capable mind.

Manic-depressive psychoses are not easily differentiated from other psychoses, especially dementia precox. In the latter disease the following seems to be an important diagnostic point: If in an individual affected with alternating outbreaks of depression and exaltation, each characteristic of melancholia and mania respectively, a change of his affective and intellectual faculties, and particularly of the first, is observed, the presumption is in favor of dementia precox. A. Gordon (*Jour. of Nerv. and Mental Dis.*, Jan., 1912).

Consciousness is clear except in the states of excitement, depression, and stupor, when it is clouded; but it is seldom entirely lost, and patients who are apparently completely unconscious and stuporous often partially appre-

ciate, and can later describe, some of the details of what occurred about them during the period of their stupor. The field of consciousness is, however, frequently decidedly restricted as a result of disturbances of the attention and apprehension and the inhibition of thought processes.

Impairment of the attention is one of the most constant symptoms. This is evidenced in a lack of interest in the surroundings, and inability to concentrate the mind or follow accurately any train of thought. In conditions of stupor and excitement there may be no evidence of attention on the part of the patient, who nevertheless perceives and apprehends in a superficial manner much that occurs about him.

Apprehension and orientation are comparatively well preserved, and apathetic patients often surprise their attendants by pertinent remarks concerning their environment. Orientation for time, place, and persons is accurate or but slightly affected except during stupor or when mental deterioration is far advanced.

False sensory impressions or hallucinations are of frequent occurrence, especially in the earlier stages, and are commonly associated with confusion of thought, delusions, and abnormalities of conduct. The hallucinations may be referred to any of the sensory channels, but those of hearing are most prominent and persisting. They are often of a grotesque or fantastic character and usually of a disagreeable nature, particularly at first; later they become less distressing as emotional indifference develops, and the patient pays little attention to them.

Memory is good in the early stages

or shows impairment only in proportion to the lack of attention; events are superficially perceived and hence imperfectly remembered. Old memories are therefore more clear than recent ones. Later, with the development of dementia, new impressions become less and less numerous, the ability to recall old memory images becomes impaired, and in the extremely demented cases only isolated fragments of memory are revealed in the utterances or conduct of the individual.

Judgment and reasoning ability, depending as they do upon attention, perception, memory, association of ideas, formation of concepts, and other mental processes, necessarily suffer from the first, and deteriorate during the entire course of dementia precox. Perceptions and experiences are incompletely comprehended and poorly analyzed; false perceptions, or hallucinations, are not recognized as such; thus, false ideas and beliefs, or delusions, originate which cannot be corrected by any proof of argument or experience. The individual in consequence is incapable of making logical decisions, fails to react rationally to his environment, does not adapt himself well to new conditions, and insight into his own mental state is wholly lacking.

The emotional states of dementia precox represent some of the most constant and characteristic symptoms of the disease. Even before its actual onset, or at least before it can be definitely diagnosed, apathy, anxious states, phases of depression and excitement, and general emotional instability are strikingly prominent. When the development of the disease is acute or subacute the emotional re-

action to delusional ideas accounts for much that is abnormal in the conduct of the individual. As dementia develops there is a gradual progressive deterioration in the emotional life, and the patient becomes more and more indifferent. He fails to react, or reacts inappropriately, evincing no feeling tone when describing his delusions of persecution or grandeur, and exhibiting apparently causeless and silly laughter or weeping, and sometimes both, almost in the same breath. The moral sense disappears; affection for family and friends is lost. Expressions of joy, sorrow, happiness, grief, affection, resentment, fear, etc., are replaced by emotional indifference to all external conditions. This apathy of the emotions may be one of the first signs in the patient's behavior to call attention to the psychosis.

In the domain of the will the manifestations of dementia precox are particularly important. The disturbances in all the other fields of mental activity tend, singly and collectively, to cause a progressive disappearance of normal voluntary activity. The absence of a complete comprehension of the environment, the poverty of thought content, the lack of interest and feeling tone explain to a large degree the conduct of the patient, who sits for hours and days listless, unoccupied, apparently day-dreaming, and exhibiting only the most primitive voluntary activities, such as walking, eating, and various stereotyped movements. Motives for action are crude and incompletely expressed, giving rise to perseveration and stereotypy. Imperative impulses, often based upon delusions and unrestrained by cerebral inhibition or judgment, are immediately acted upon and give rise to

impulsive acts of the most sudden, inexplicable, and often violent character. Abnormal functioning of the will also gives rise to the states of negativism, catalepsy, and hypersuggestibility.

While all of the elements of mental activity are affected in varying degrees in dementia precox, the dissociation of their functions is more evident than the actual impairment, and this dissociation or inco-ordination of mental processes has been termed intrapsychic ataxia, or schizophrenia (splitting of the psyche). This inco-ordination of thought is especially manifest in the separation of thought content and emotional reactions, *i.e.*, unreasonable and unreasoning emotional reactions coexistent with an intellectual state that would normally control them, or apathy when emotion would be expected. The patient speaks of the death of his dearest friend with an appearance of feeling; he laughs or weeps and exhibits anxiety or temper without being able to give any reason for so doing. The whole attitude and behavior of the patient impresses one as being incongruous.

Further evidence of mental dissociation is shown in the statements of the patients, who frequently complain that all of their actions are under the control of another. The incongruity in behavior can sometimes be traced by psychoanalysis to hidden complexes or feeling states, which are more or less completely separated from consciousness and manifest themselves in the anomalous emotional reactions. These complexes are undoubtedly of great importance in the determination of the symptomatology of dementia precox.

The physical symptoms frequently, although not constantly, found in the early stages of dementia precox are of some significance. Among the most important of these are digestive disorders, loss of weight at times amounting to emaciation, oily or sallow complexion, acneiform eruptions, headache and other subjective pains, rapid heart action, increased tendon reflexes, dilated pupils, and vasomotor disturbances, such as cyanosis and sweating of the extremities, dermatographia, and flushing of the face. Menstruation may be irregular or completely suspended in the female cases. Low physical vitality is quite characteristic of the disease; resistance to infection is diminished and tuberculosis is a very common complication and frequent cause of death. Many of the cases gain rapidly in flesh after the early stages without corresponding mental improvement.

As has already been stated, the types of dementia precox usually described are the *hebephrenic*, the *catatonic*, and the *paranoid* forms. This division of the cases is somewhat artificial and incomplete, as many individuals exhibit symptoms common to all forms. The classification is practical, however, as the average case conforms fairly well regarding the majority of symptoms present with one or other of the special types.

**Hebephrenia.**—The onset of this form of dementia precox is usually gradual and the patient may not come under medical observation for several years. The disease occurs at an earlier age than in the other forms, and frequently develops at or soon after puberty. Most of the cases begin before the 25th year. The individual, predisposed from childhood,

apparently unable to withstand the rapidly increasing complications and responsibilities of life, especially the new instincts and feelings accompanying the maturing of sexuality, succumbs to the strain, and the result is a slowly progressive mental deterioration which may reach any degree of dementia. It has often been said of these patients that they are "shipwrecked on the cliffs of puberty." Previous to any definite dementia the individual generally complains of headache, sleeplessness, palpitations, and various neurasthenic symptoms. He loses interest in his surroundings and occupation, and spends much of his time in listless day-dreaming. Capacity for continuous effort is lost, and, as a result of inefficiency, he frequently changes his position of employment, making the excuses that the work is too hard, that he is unfairly treated, that he does not feel well or strong. At the same time a mental and physical examination reveals nothing characteristic. The mentality is good, and may even be much above the average. There is often observed, however, what has been termed the "shut-in" personality, characterized by seclusiveness, shyness, introspection, and self-absorption. The patient lives within himself, taking as little part as possible in the affairs of those about him. This "shut-in" character may have been present in the individual since early childhood, and he may have been recognized as "peculiar," "odd," or "not like other children." In the physical examination there is nothing found to account for the various subjective complaints of the patient excepting evidence of a diminished resistance and vitality in the muddy complexion, the coated

tongue, and sluggish bowels; the cold, clammy hands and fluctuating color of the face, indicative of a general loss of vasomotor tone or stability.

One of the earliest and most characteristic of the definite symptoms of hebephrenia is the change in temperament and in the emotional life of the individual. Periods of restlessness or excitement recurring at intervals or alternating with states of depression, irritability, obstinacy, or total indifference to everything making up their environment replace normal and rational reactions. This is evidence of the beginning of the development of mental dissociation, or splitting of the psyche, which is one of the most characteristic processes in dementia precox. While the intellectual processes are but little affected the emotions are distinctly abnormal. The patient shows passion without cause, or is apathetic in the face of real calamity. Morality and the sense of responsibility are affected, with the result that not only are obligations neglected, but offenses are committed against moral and civil law. Masturbation and promiscuous sexual intercourse are frequent, and petty crimes make patients of this disease common inmates of the prisons.

During the first few months or even years of the disease nothing more may develop. On the other hand, the above symptoms are not constant and may be subject to remissions during which the patient appears to be entirely natural. But with each succeeding recurrence the symptoms tend to become more and more pronounced, especially after any severe mental or physical stress. In some few cases the disease is abortive, and it may be arrested for a long time or

even permanently at any stage, leaving the individual more or less incapable, irresponsible, and inefficient. Such cases go to make up a large percentage of the chronic vagabonds, eccentrics, prostitutes, and criminals. In the majority of cases, however, the disease develops more or less insidiously and new symptoms appear from time to time. Hallucinations develop, manifesting many variations and inconsistencies, and are usually of a disagreeable nature. The patient hears himself being called vile names, sees impossible monsters and evil spirits, or experiences loathsome sensations through the avenues of touch, taste, or smell. At times, however, the hallucinations are agreeable; music is heard, angels are singing to him; he is addressed by the voice of God, which directs and commends his conduct. Mysterious messages are received and visions of heaven and hell are seen. At first the patient may be disturbed and depressed or elated by these hallucinations, which are constantly changing, but later emotional apathy develops and they are discussed with no sign of feeling or passion. Delusions may be associated with the hallucinations or they may occur independently of them, and often have a hypochondriacal or self-accusatory character. The patient believes that he has destroyed his life by self-abuse; that he is a criminal, for which he must be punished; that he has committed an unpardonable sin, for which he is to be eternally damned. The organs of his body are rotting away; he has no brain, no stomach; he cannot hear, see, eat, feel, or even think. Delusions of persecutions may occur and the patient believe himself to be the

object of a plot; he is being watched, followed, tormented. An illustration of the delusions of hebephrenia occurred in the case of a young unmarried woman who was admitted to the medical ward of a general hospital apparently suffering from neurasthenia. Shortly after her admission she confided to the physician that she had come to the hospital to escape from her relatives, who had tried to poison her. There was no disturbance of consciousness, memory and orientation were good, and her story was consecutive and almost convincing. She soon showed evidence of experiencing auditory hallucinations of a persecutory character, and a few days later accused the hospital interne of having raped her in the presence of the nurses and other patients. Although she sincerely believed that she had been violated, her resentment was limited to a querulous complaint to her friends, and she treated the interne much the same as before. A few cases of hebephrenia exhibit delusions of grandeur, but these are exchangeable, transient, and poorly systematized. The patient considers himself to be a most important individual in the world of intellect, politics, finance, or religion; he is a special envoy of God; he is Christ; he is God Himself. The lack of permanence and of attempts to support his claims by logic separates these cases from the more systematized delusions of the paranoid form.

Throughout the course of the disease, periods of excitement are common which may be difficult to distinguish from the phases of manic-depressive insanity. In the periods of excitement there is sleeplessness, motor restlessness, loud talking, etc.;

in the depressed periods, dejection, hypochondriacal delusions, and suicidal tendencies. The true nature of these episodes is especially difficult to recognize in the absence of any previous knowledge of the case; but even during the excitement or depression there is almost always a significant lack of harmony between the thought content and the emotional reaction.

As has been said, there is from the first a progressive mental deterioration. This is early evidenced by a lack of interest in the environment, the field of consciousness being largely restricted to personal considerations. Facts relating to the surroundings are incompletely assimilated because of lack of attention and interest. The thought content becomes more and more limited and superficial, and later disconnected and desultory. The dilapidation of the train of thought is manifested by senseless and irrelevant statements in the course of otherwise intelligent and coherent conversation. The most absurd statements are made without any appreciation of their inconsistency. The speech becomes verbose and pedantic, and is frequently interspersed with senseless coined words (neologisms). There is a marked tendency to the endless repetition of certain words or phrases (verbigeration), and when the dementia is well advanced the speech becomes a literal hodge-podge of disconnected expressions without any grammatical construction, to which the French have applied the term "word-salad."

The behavior undergoes a characteristic and progressive change; the manner is childish, silly, affected, and gives the impression of insincerity. Silly laughter is particularly characteristic

and occurs without the least provocation or relation to external circumstances. Habits and mannerisms develop and the patient assumes unnatural attitudes, which are maintained for hours at a time. Stereotyped movements, such as pacing the room, rubbing the hands together, stroking or tapping objects near at hand, are also characteristic. Sudden changes in manner, April weather behavior, and the most unexpected and inexplicable impulsive acts go to make up the conduct of the typical case of this disease. At the same time the personal appearance is neglected, habits become slovenly and filthy, and all sorts of foolish acts are performed.

Judgment and discrimination are affected early, and as the dementia progresses become badly disorganized. While the patient is in a protected environment with no responsibility or need for action, this disturbance may not be fully appreciated; but if placed in a strange environment upon his own resources, where the necessity for decision and action is imperative, this defect in character becomes strikingly apparent and the subject drifts into some public institution, be it hospital, asylum, or prison. Under these conditions everything is accepted by the patient largely as a matter of course, and if protest or complaint is made it is half-hearted and lacks sincerity; he is as contented in confinement as at liberty or even more so, as there is less call for action or decision on his part.

In the last stages of the progressive cases the mentality degenerates to almost absolute vacuity, and the existence becomes purely vegetative. The patient is mute or utters only a few senseless or unintelligible words. He does not respond to questions or give any evi-

dence that they have been heard. He must be led to meals, washed and dressed, and passes excreta in the clothes or bed. Orientation, the last faculty to be lost, finally disappears, and the condition closely resembles that of complete idiocy, from which it can be differentiated only by the history and by the occasionally momentary flash of the wreck of intelligence.

Exacerbations or episodes are prone to occur from the beginning to the end, and these seem frequently to be associated with such debilitating conditions as exhausting fevers, hemorrhage, physical trauma, and the menstrual periods and childbearing in women. As a rule, the dementia becomes more marked after each exacerbation. On the other hand, remissions may occur, and the patient be apparently normal for an indefinite time. A complete arrest of the disease may occur at any stage, the active symptoms disappear, and the patient be left in a state of passive inefficiency for the rest of his life, the degree of inefficiency depending upon the stage at which the process has been arrested. It may be taken as a well-established rule, however, that a definite dementia, or actual intellectual loss, once established is permanent.

According to Kraepelin, about 75 per cent. of the cases of hebephrenia reach a profound degree of dementia and are utterly unable to do any work or even wait upon themselves. About 17 per cent. reach a less-advanced stage and are able to perform routine work under supervision, and in about 8 per cent. recovery is apparently complete and the patient finds profitable employment, free from all active symptoms of the disease. But a careful study of even these cases will usually reveal a limitation of initia-

tive, constructive mental ability, and decision of character. "The patients have been unable to realize their ambition. Young men and women whose academic or collegiate courses have been interrupted by the psychosis find themselves unable to enter into active business or professional life. These patients are able to care for a farm or a small business where there is little demand for intellectual work. In this way we lose sight of the mental shipwreck following dementia precox, because enough mental capacity is retained to permit them to maintain the battle of life in their chosen narrow field."

The course of the disease is variable, but it is generally progressive and less subject to remissions than the catatonic form. In some cases the progress is rapid and dementia is far advanced within a year after the onset. In others the same stage is reached only after several years.

It is characteristic of the hebephrenic form of dementia precox, in contradistinction to the catatonic and parauroid forms, that the emotional and intellectual deterioration are the main features, and are but little complicated by the occurrence of the more active symptoms common in the other forms, such as negativism, catalepsy, stereotypies, persistent and systematized delusions, etc. Many or all of these symptoms may appear, however, in varying degrees, rendering a definite line of demarcation at times impossible.

**Catatonias.**—In the catatonic form of dementia precox are included those cases prominently manifesting certain striking symptoms, chief among which are periods of so-called catatonic excitement and catatonic stupor, negativism, hypersuggestibility, stereotypies,

sudden and violent changes in behavior, etc., in addition to the general tendency toward progressive mental deterioration, and usually ending in advanced dementia. Remissions occur more frequently in this form than in either of the others, and complete arrest of the disease is more often observed. Some of the special symptoms peculiar to catatonias deserve further consideration before a discussion of its course and symptomatology is continued.

Negativism has been subdivided into external and inner negativism, and external negativism into active and passive negativism. External negativism is that condition of mind which induces the patient to refuse to do that which he is expected or requested to do (passive negativism) or even to do exactly the opposite (active negativism). Negativism of the will and of the intelligence (inner negativism) signify inability on the part of the patient to do that which he wills to do, and the tendency to think the opposite thoughts to those which would naturally occur. It is difficult to explain all the phenomena of negativism, but a recent monograph by Bleuler (1912) analyzes some of the mental processes operative in their production. According to this author, the predisposing factors include ambitendency and ambivalency, by which each tendency is endowed with a counter-tendency, and each feeling tone or thought simultaneously with a positive and negative character. These processes are, in a measure, normal processes, as all decisive action represents a choice between more or less opposing conditions: we say that it is warm because we know that it is not cold; we comply with the request of a friend because we do not wish to refuse. But our action is based upon a clear ap-



preciation and balancing of the alternatives. In the catatonic, however, the lack of clearness and imperfect logic of thought processes, and the mental incoordination or splitting of the psyche, destroy the faculty of making reasonable decisions, and the wrong impulse is as likely to be acted upon as the right one. Furthermore, the pathological irritability of the patient and his tendency to withdraw himself into his own world of phantasy render all outside influences disturbing and intolerable interruptions. The result is a whole deluge of negativistic actions of many types and degrees, which flood the symptomatology of catatonia. When this condition is present the patient closes his mouth tightly when asked to show his tongue, is mute when spoken to, refuses to eat his own dinner, and then steals that of his neighbor, and resists all kinds of interference. Increased muscular tension and rigidity is an almost constant feature. Not infrequently the patient becomes active in his opposition to the suggestions of others, undresses himself after being forcibly dressed, tears his clothes when requested not to tear them, or puts his hand behind him when a handshake is proposed. He may show irritability by suddenly striking his tormentor, but quickly resumes his former passive state.

Hypersuggestibility is also a factor in determining the conduct of the catatonic, and may alternate with negativism or be associated with it to some degree. This is manifested by a tendency to obey automatically all requests or directions (command automatism), to repeat words or phrases spoken by others (echolalia), or to copy the movements which he sees others perform (echopraxia).

While negativism and hypersuggestibility are opposite in their manifestations, they are based upon a similar mental state, which favors either unreasoning opposition or equally unreasoning obedience to suggestions from without. The presence of both tendencies existing simultaneously in one patient may be demonstrated in states of catalepsy in which certain suggestions are opposed and others obeyed. Closely related to command automatism is the condition of *flexibilitas cerca*, or waxy flexibility, in which state the patient resembles a jointed manikin that can be placed in any posture, no matter how grotesque or uncomfortable, which is retained until moved into another position or the muscles become completely fatigued.

Stereotypy is a disturbance manifested by the maintenance for long periods of peculiar attitudes, or the indefinite repetition of certain movements or of words, phrases, or sentences. This disturbance arises from an interference of thought and action through a blocking of the will. The thought or action is arrested without being fully expressed and the patient remains in a fixed attitude with increased muscular tension and rigidity (stereotypy of attitude); or a fragment of the expression is repeated indefinitely by automatic movements or the reiteration of set forms of speech (stereotypies of movement and speech). It is by this process that the mannerisms, tics, and antics so characteristic of catatonia develop.

The first appearance of the mental symptoms is usually somewhat later in catatonia than in hebephrenia, but nearly always occurs during adolescence or early adult life. In a few

cases it develops in childhood. The onset is, as a rule, subacute, but is subject to many variations. The physical symptoms are of the same type as those of the hebephrenics, but are more pronounced. Before the development of definite mental symptoms there is often a period of restlessness, irritability, neurasthenic and hysteriform symptoms, and at times an indefinite feeling of apprehension on the part of the patients, a feeling that something is wrong with them or a fear that they are going insane. This was particularly marked in a case of personal observation in which the patient, a young woman, early in the initial stage manifested a constant fear that she would be affected as was her sister, who died in an asylum. Among the early symptoms, those of a hysterical nature deserve especial mention. Hysteriform convulsions, fainting attacks, functional anesthesias, and paralyses are not infrequently met with, and are prone to lead to mistaken diagnosis until the symptoms characteristic of catatonia are recognized. Another source of difficulty in recognizing the first manifestations of catatonia arises from the fact that many of the patients suffer repeated recurrences of attacks of excitement or depression with lucid intervals, which are almost impossible to distinguish from manic-depressive insanity. Urstein (1912) has called particular attention to this fact in an extensive monograph on catatonia, and describes cases in which repeated attacks of excitement or depression or circular phases have recurred at intervals over a period of many years before the typical and characteristic features of catatonia were evident.

In some cases the mental syndrome

for a considerable length of time is that of hebephrenia, the distinguishing features of catatonia appearing later and determining the type of the disease. At times the development is rather rapid, especially after illness or conditions causing mental or physical exhaustion. After a short period of nervousness or irritability, a certain abnormal muscular tension is manifested by the stiffness and awkwardness of attitudes and movements, and the patient pays little attention to his surroundings. When spoken to he answers briefly, stops speaking in the middle of a sentence, or whispers with obvious effort. The field of consciousness becomes more and more restricted, the reaction to the environment becomes less and less and is eventually entirely absent, and the patient passes into the so-called *catatonic stupor*, which is one of the most characteristic conditions of this disease.

Catatonic stupor is brought about largely through the action of negativism, hypersuggestibility, and automatism. In this state the patient may lie for days, weeks, or even years at a time, giving no evidence of consciousness of his surroundings and at times failing to respond to any painful stimuli that may be applied to his body. This stupor is, however, more apparent than real, for the patient actually apprehends much that transpires about him, frequently remembering and describing, after recovery from the stupor, events to which he seemed entirely oblivious at the time of their occurrence.

During the stuporous state passive negativism is often strongly in evidence; the eyes and mouth are held tightly closed when attempts are

made to examine them, all efforts of approach are resisted, and forced feeding is not infrequently required. *Cerca flexibilitas* may replace the negativism or alternate with it, the patient exhibiting a waxy pliability in place of resistance. Mutism is usually continuous. When the pseudostupor is less intense stereotypies are manifested in the persistent repetition of various purposeful but useless movements or the endless reiteration of senseless words. Automatic mimicry of the speech or movements of others (echolalia and echopraxia) may occur at this stage, but are usually of short duration. Notwithstanding the fact that in catatonic stupor thought processes are inhibited, consciousness and orientation seriously affected, and all of the normal mental activities dormant, this state may persist for long periods of time, even for years, without marked mental deterioration being evident after it clears up.

Catatonic excitement is a state that may develop at any stage of the disease, and often follows or precedes a state of depression or stupor. It is characterized by psychomotor activity, violent and impulsive actions, stereotypies, and a reckless disregard for everything. It often appears suddenly and the patient rushes about, assaults anyone in his path, destroys property, shouts, sings, laughs, cries, smears himself with filth. All sorts of absurd antics are performed, such as hopping about on one foot, turning somersaults, and standing on the head. Speech is loud, monotonous, and incoherent; it is especially characterized by the constant recurrence of the same words intermixed with a meaningless jumble, and is often continuous for hours at a time (verbig-

eration). Obscene words, peculiar grunts, and other inarticulate sounds are frequently interspersed. During catatonic excitement, as in the stupor, the patient is indistractable, paying little heed to the action of others or to what is said to him. The excited state may develop less stormily and exhibits all possible variations in degree in the different cases.

The states of stupor and excitement recur or alternate irregularly and last for variable lengths of time, the former occurring more frequently and usually having a longer duration than the latter. In the time intervening between these states the symptoms are similar to those of the hebephrenic, and frequently they are more accentuated. Hallucinations are vivid and changeable, delusions are wild and absurd, and the conduct subject to violent fluctuations. One patient may suddenly assault another without evident provocation, either from pure impulse or because he imagines he hears the other calling him vile names. At this time consciousness and orientation return, and memory is surprisingly good, especially for remote events, although it is not uncommon for the patient to recall many incidents that happened during the stupor or excitement. The train of thought is disconnected, superficial, and introspective, and the emotional attitude is more or less out of harmony with the other mental processes. Stereotypies are usually present and mannerisms develop, consisting of facial grimaces, peculiar attitudes of gait and station, grotesque gestures, stilted manner of speaking, etc. The attention of the patient is difficult to gain or hold, and his answers to questions are characteristic-

ally irrelevant (the "Vorbeireden" of the Germans). The behavior is subject to great variations, from vacuous silliness or clownishness to extreme irritability and sudden outbursts of temper and acts of violence. The conduct of the catatonic most typically illustrates the April weather behavior of insanity.

The speech and especially the writing of the patient mirror his mental processes, showing the poverty of thought content, the superficiality and isolation of ideas. The writing is characterized by verbigeration, absence or excess of punctuation, numerous underlinings, and a lack of all logical connection or grammatical construction.

A considerable number of cases which he observed convinced the writer that dementia precox is characterized by such marked peculiarities in chirography and in composition of letters that by examination of the latter and other writings by these patients the diagnosis can be made quite definitely. In 1904 he published an article on the handwriting of the insane in which he showed its main characteristics in dementia precox. Similar work was done in 1905 by Rogues de Fursac. Some of the patients exhibit a perfect mania for writing. They fill page upon page with disconnected phrases, repeating themselves in a stereotyped way. They copy very willingly all that may happen to come under their notice without any sense of practical value. Other patients, however, feel no desire for writing, but will write when asked to do so. Finally, a third class of patients become unable to write. From the viewpoint of chirography their handwriting is marked with great carelessness, includes a mass of corrections, and is illustrated with drawings of extremely naïve character. There is no regularity in the arrangement of lines in letters; the

size of letters varies extremely, the writing being either very small or very large in different parts of the line or page, or new forms of letters are sometimes created. Obraztsoff (Roussky Vratch, March 24, 1907).

The course of the catatonic form of dementia precox is sometimes rapid, and severe mental deterioration appears within a few months or a year from the time of onset. In such cases the symptoms are usually active from the first; stupor or excitement occur early and persist or alternate; remissions are brief or absent altogether, and emaciation becomes extreme. When death occurs it is caused by intercurrent affections, of which tuberculosis is the most frequent. Other infections are also induced by the low vitality of the patient. The stage of dementia may persist indefinitely, and resembles that of hebephrenia except for the existence of more pronounced irritability, stereotypies, and mannerisms. The catatonic stupor may last for very long periods, even for years, and finally clear up, leaving slight mental loss. Lack of initiative, inefficiency, and dissociation of emotion and intellect can, however, be detected in some degree. Acute exacerbations separated by long intervals of quiescence may induce dementia only after many years. Remissions are prone to interrupt the progress at all stages of the disease, and vary in duration from a few hours to many years or even permanent arrest of the psychosis.

Kraepelin has found that about 49 per cent. of the cases of catatonia end in pronounced mental deterioration, about 13 per cent. apparently recover, and the remainder, or 28 per cent., attain various degrees of less-advanced dementia. As was stated regarding

hebephrenia, so with catatonia, the cases of apparent recovery, when subjected to severe tests, reveal limitations in mental capacity compared to their previous ability.

**Paranoid Forms.**—The distinguishing features of the paranoid forms of dementia precox are the occurrence and persistence of vivid hallucinations, and the existence of delusions which are retained, elaborated, and systematized, together with clear consciousness, a long course, and a gradually developing dementia. Remissions are infrequent and recovery practically never occurs, although the psychosis may remain stationary for long periods of time. The age of onset of the mental symptoms is, as a rule, later than that of either of the preceding forms, and a majority of the cases show the first signs of the disease after the age of 25 years.

Eccentricities and "shut-in" personality cannot infrequently be traced to early life. Seclusiveness and morbid and antisocial mental attitudes mark many of the predisposed individuals. The onset is usually more gradual and prolonged than in the other forms, but is characterized by many of the same conditions. Restlessness, suspiciousness, and hypochondriacal tendencies are particularly to be noted, and the indefinite fear of impending calamity and the feeling that something is wrong with the mind, to which reference has already been made under the heading of Catatonia, are especially important in their relation to the paranoid form of dementia precox. In the course of time mild delusions of persecution make their appearance; the patient believes that he is being slighted or unfairly treated by his associates or employer;

his fellow-workmen are conspiring to deprive him of his position by means of tricks, and communicate with each other by secret codes concealed in the most casual movements and glances. The simplest remarks of others are thought to contain ulterior significance, and those about him can read his thoughts and know all the details of his past life, especially that portion which he wishes to conceal. This knowledge is spread and used to his detriment. Secret social organizations take it up and plan to drive him out of the country. At this time the patient may complain of peculiar feelings in the head and confusion of thought; he is greatly worried, restless, and depressed. He cannot eat or sleep and thinks of nothing but his troubles. He becomes unusually scrupulous and overconscientious; he searches his past conduct for misdeeds and endeavors to atone for trivial or fancied offenses. Consciousness is clear, and the details of delusions are described and explained by a combination of actual facts and illogical interpretations. The patient will admit each argument proposed to discredit his insane ideas, but nevertheless fails to be convinced of their falsity. The delusions increase and the persecution becomes intolerable to the patient: he is sure that certain individuals, or all of the community, are in league to destroy him, to burn him at the stake, to change him into a negro, or to make him walk naked through the streets. He seeks protection from his enemies through application to legal authorities, or to escape from them by traveling to a distant part of the country. Here he finds no relief, but discovers that strangers know all about him, proving this to himself by the gestures which they

make when they meet him. He returns home to find that his very best friends have turned against him and are in sympathy with his enemies. In desperation he may attempt suicide or take the law into his own hands and try to kill some acquaintance whom he believes to be chiefly responsible for his persecution. When confined in an institution he may be temporarily relieved to some degree of his anxiety by a feeling of security from his enemies; but the delusions persist and soon the officers and attendants join the general organization of society against him. All kinds of ingenious and fantastic methods are devised by his enemies to torment him. Hallucinations frequently appear early and correspond closely to the delusions. Sometimes the hallucinations precede the delusions, which then may show evidence of being based upon them. Voices of enemies revile and threaten the patient; putrid vapors are forced into his room; he detects poison in his food, sees diabolical forms about to attack him, or feels electric currents and burning acids applied to his body, all of which forms of torment are details of a systematic plan on the part of his enemies.

In some cases the delusions and hallucinations are variable and change frequently, in others they are more consistent and fixed, but in all there is a marked tendency to systematization more or less elaborate. Following the persecutory stage many of the patients pass more or less gradually into one of exaltation, in which the delusions are largely or completely of a grandiose type. In his hallucinations the patient may hear himself referred to as an important personage; or his persecution by such influential enemies may lead him to infer that he, himself, is great.

The idea is adopted and he assumes the manner of a millionaire, a king, or Jesus Christ, and the mass of his delusions becomes correspondingly appropriate, but do not lose their persecutory character at once. Although his rights are being withheld from him, he is more or less contented and is confident of their final restoration.

The appearance of a marked mental deterioration varies greatly in different cases; in some dementia begins to develop almost from the first; in others only after several years is it noticeable. With its incidence the hallucinations and delusions lose their active character, and tend to fade and disappear as it develops. The terminal demented state of the paranoid form resembles that of the other forms of dementia precox, although fragments of the delusions often remain and the patient remembers that he is an admiral, a prince, or the Messiah.

The term *dementia paranoides* has been applied by Kraepelin to those cases running a comparatively acute course, presenting many incoherent and changeable delusions, and dementing early. In another group of cases the progress of the disease is very slow and only after many years is an advanced state of dementia reached. Remissions are infrequent and are seldom characterized by a complete absence of delusions, although these may be difficult to elicit on account of the suspiciousness and reticence of the patients. Recovery does not occur.

Many of the cases present certain catatonic symptoms, such as periods of excitement, mannerisms, and stereotypies, but these are usually not prominent.

In the earlier stages the emotional reactions and the conduct correspond to

the delusional mental state. The patient is anxious, depressed, indignant, revengeful, or exalted, and his behavior parallels his mood. Later, dissociation of thought content and the emotions becomes manifest in the conduct, and the "princess" contentedly washes the dishes or the "millionaire" meekly begs a chew of tobacco.

In the above descriptions of the different forms of dementia precox the symptomatology of the "typical case" has been fairly closely adhered to, but, as is a matter of actual observation in many other diseases, so with dementia precox, the typical case is not the average case. The clinical manifestations of each of the special forms are prone to overlap those of the other forms, and it is frequently difficult to determine to which group a given case belongs.

Practical experience teaches us that no sharp differentiation can be drawn between the various forms of dementia precox—hebephrenia, catatonia, and dementia paranoides. Every now and then we meet with cases of hebephrenia in which passing motor phenomena, convulsions, transitory rigidity, or stereotypy is noted, or again cases of dementia paranoides in which like features cause an approximation to catatonia. It is often difficult to draw a differentiation between a dementia paranoides and a phantastic paranoia just as it is difficult always to make an absolute differentiation between the latter and the paranoia of Magnan, the "combinirte" form of Kraepelin. F. X. Dercum (Jour. Amer. Med. Assoc., Feb. 4, 1905).

**DIAGNOSIS.**—While many of the various symptoms of dementia precox are very characteristic and striking, none are pathognomonic of the disease, since any of them may occur in the course of other psychoses. The

association of the different symptoms, and the course of the disease tending toward loss of emotional tone and mental deterioration, are of fundamental importance. It is frequently impossible at a given time to make a positive diagnosis, and it is only after a significant history is obtained or subsequent developments are followed that the case can be satisfactorily classified. The conditions from which it may be necessary to distinguish dementia precox include neurasthenia, hysteria, psychasthenia, manic-depressive insanity, general paresis, epileptic insanity, paranoia, psychoses due to infections, exhaustion or intoxications, and congenital mental inferiority.

In the early stage of dementia precox many neurasthenic and hysteriform symptoms indistinguishable in themselves leave the diagnosis in doubt until the appearance of unusual silly or illogical behavior, limited working efficiency, mannerisms, delusions, changes in character, or the more active symptoms of the disease reveal the nature of the process.

In catatonic excitement the manic form of manic-depressive insanity may be difficult to exclude. Favoring catatonia, however, are the presence of verbigeration, stereotypies, poverty of thought content, dissociation of ideas, and disregard of environment. In contrast to these symptoms the active emotions, versatile behavior, flight of ideas, momentary distractibility, and repeated periodic attacks without mental deterioration indicate mania. Catatonic excitement may, however, be exhibited in cyclic recurrences over a period of many years before marked dementia makes its appearance (Urstein).

The depressed states so common in early dementia precox are readily mistaken for the depressed phase of manic-depressive insanity, and, as with excitement, the dementia may be delayed until after several attacks, increasing the difficulties of the diagnosis. Significant symptoms of the depressions of dementia precox are inconsistent emotional reactions, absurd hypochondriacal delusions, stereotyped attitudes and movements, and negativism. This last must be carefully distinguished from the retardation of thought and the desire to be left alone observed in melancholia.

While many of the symptoms common in dementia precox are not infrequently observed in general paresis, including negativism and *cereæ flexibilitas* in exceptional cases, the parietic process is indicated by Argyll-Robertson pupils; increase, diminution, or inequality of knee-jerks; tremors, especially of the tongue and facial muscles; speech characterized by the imperfect enunciation of long words, and the commission of obvious errors in simple problems of mental arithmetic.

In dementia precox the pupils are on the average larger than normal and fluctuate in their size quickly and often. Whether permanent disturbances of the light reflex occur is uncertain; in rare cases of catatonic stupor a catatonic pupillary rigidity has been transiently observed, associated with mydriasis, miosis, or an oval or linear pupil. Such changes of form may also occur independently of the catatonic pupillary rigidity and may affect only one eye. The pupillary anomaly pathognomonic of dementia precox is the absence of the pupillary restlessness, of the psychoreflex, and of the reflex dilatation of the pupil to sensory irritation while the light reflex is preserved. This

symptom is constant when it once exists; it occasionally develops in the early stage of the disease, it is present in more than half of the cases at the height of the disease, and is almost never absent in the very bad cases. During this development the dilatation of the pupils to sensory irritation becomes lost, the same as the pupillary restlessness and the psychoreflex. The diagnostic importance of these signs rests upon the fact that they are almost never present in other processes of similar nature caused by organic brain changes, aside from dementia precox, while they are present in healthy persons, as well as in those with manic-depressive insanity or other functional mental diseases. Bumke (Münch. med. Woch., Dec. 20, 1910).

Ocular signs and symptoms of dementia precox as observed in 115 consecutive cases. The fundus changes seen clinically are divisible into three groups: 1. Congestion of the disks, hyperemia, and edema; dilated, dark-colored veins; slightly contracted arteries, and blurring of the edges of the disks, all varying in degree. These changes constitute a low grade of perineuritis of the optic nerve. 2. Congestion of the nasal side, with temporal pallor of the disks, dilated veins, contracted arteries. 3. Pallor of disks, dilated veins, contracted arteries. These changes constitute anemia and partial atrophy of the optic nerve. The pupillary reactions to light and accommodation were sluggish, and the sensory pupillary reflexes negative in a large majority. The sensitiveness of the cornea was diminished in a very large majority. The visual color fields were concentrically contracted in all the cases. The changes in the optic disks, pupils, visual fields, and corneal sensibility form a new syndrome that they did not find in any other form of insanity, imbecility, or idiocy. Their interpretation of these findings is as follows: 1. They indicate that dementia precox is attended by such an early and constant syn-



drome of alteration of disk, visual field, pupil, and corneal sensibility as materially to aid in the diagnosis, especially from the manic-depressive group, acquired neurasthenia, hysteria, and the various forms of imbecility and constitutional inferiority. 2. The syndrome supports the theory that dementia precox is an autotoxic disease, and that the poison is primarily vascular, which finally induces neuronc degeneration. It points to a toxin of some sort, which is either a metabolic defect in the tissues (ductless-gland defect), or, what seems more probable, a poison generated in the liver or in the gastrointestinal tract. 3. The syndrome is of prognostic value, as the severer grades of eye changes are found in the more rapidly deteriorating cases. 4. The optic-nerve lesion is quite in accord with our best knowledge of the pathological anatomy of dementia precox in other tracts of the brain. Tyson and Clark (*Archives of Ophthalmol.*, May, 1912).

Of conclusive significance would be positive Wassermann reactions of the blood and cerebrospinal fluid, with lymphocytosis and increased globulin content of the latter; these conditions, almost constant in general paresis, are not present in uncomplicated dementia precox.

The serum of patients with dementia precox and manic-depressive insanity inhibits the hemolytic action of cobra venom, while other serums do not possess this property. The writers examined 400 serums, including nearly 50 persons with these mental affections, and the reaction occurred positively in this group, as also in persons whose parents had had these affections, and it occurred in none of the others. Both for diagnosis and from the forensic standpoint this announcement is important, and it also throws light on the nature of insanity. They call the phenomenon the psychoreaction. In one instructive case the Wassermann test was constantly

negative and the psychoreaction positive, confirming the clinical diagnosis of tabes and manic-depressive insanity based on three weeks' study of the dubious case; paralytic dementia had been first accepted. The psychoreaction was positive also in persons free from circular insanity, but with a history of it in their family. The reaction does not occur with the cerebrospinal fluid. H. Much and W. Holzmann (*Münch. med. Woch.*, May 18, 1909).

Examination of the blood in 150 cases of dementia precox, the blood being extracted from the ear-lobe, fixed in methyl alcohol, and colored with hematoxylin-eosin or with Giemsa solution. The following results were obtained: (1) Lymphocytes: small (about the size of erythrocytes) wound cells composed of large nuclei and only a thin covering of plasma. In some of these the plasma mass is enlarged. (2) Large mononuclear cells. They are three times as large as the above-named, and have plump, rounded, or horseshoe-shaped nuclei, which color faintly. (3) Polynuclears or neutrophiles with lobulated or broken-up nuclei and rich protoplasm (leucocytes in a narrower sense). (4) Eosinophiles, which are similar to neutrophiles, but in which the protoplasm is filled with coarse granules, which greedily absorb the acid coloring matter.

In comparing the percentages of these different forms with the normal percentages, there was found to be in dementia precox a notable decrease of polynuclears. In no case did they attain the normal quantities (lymphocytes, 20 to 25 per cent.; polynuclears, 70 per cent. or over; other cell forms, 2 to 4 per cent.), but were in every instance much below normal, in some cases only being found in half-quantities. This decrease was accompanied by an increase in all the other cell forms, the mononuclears and eosinophiles increasing with the lymphocytes, and sometimes attaining double their normal quantity. In cases of other men-

tal diseases tested the findings were mixed. Age and sex had no influence in the change of blood condition found. It is not certain, however, whether this change was varied according to different forms of dementia precox. It is indicated that a high number of eosinophiles generally accompanied catatonic symptoms. These observations clearly show the existence of definite blood changes in dementia precox. Heilemann (*Allg. Zeit. f. Psych.*, Bd. lxxvii, Nu. 3, 1911).

Epileptic insanity may resemble the excited or the depressed states of dementia precox, but the stereotypies, mannerisms, and negativistic behavior are usually more marked and more constant in the latter. A knowledge of the previous history of the individual is often sufficient to clear up the diagnosis.

Since the line of demarcation between paranoia and the paranoid forms of dementia precox is not well defined and varies according to the different observers, the differential diagnosis between these conditions may be to some degree a matter of opinion. It is significant that when this class of patients is carefully observed over a long period of time the number of the cases of paranoid dementia precox increases and paranoia is proportionately diminished; thus, while paranoid precox is common, true paranoia is a comparatively rare psychosis, even in the larger hospitals for the insane. It is a slowly developing disease in which the delusion and hallucinations are comparatively uniform and fixed, and they are concealed by the patient or discussed by him with much plausibility and logic. They are definitely systematized and permanent, persisting for many years, during which time they are elaborated

and lived up to by the patient. Although paranoia is incurable, it runs its interminable course without the development of dementia. In paranoid dementia precox, on the other hand, mental deterioration is an essential part of the process.

In the psychoses associated with states of exhaustion and with infectious diseases the symptoms may be confused with those of the active states of dementia precox, but they usually subside with or soon after the recovery of the physical condition. It is also true that exhaustions and infections occasionally act as exciting factors in the precipitation of dementia precox, and it is possible to gain an accurate estimate of the mental derangement in such cases only after prolonged observation.

In some of the toxic psychoses, especially those due to alcohol, difficulties in diagnosis may arise. The hallucinations and delusions of acute alcoholic hallucinosis in which memory and orientation are preserved, and the delusions of persecution or exaltation of alcoholic paranoia, present phases of similarity to some of the manifestations of dementia precox. Nevertheless, the composite clinical picture of each of the types of alcoholic insanity is essentially different from that of dementia precox, and the history of the case usually removes any difficulties.

When knowledge of the previous mental condition of the individual is lacking, it is necessary to distinguish congenital delinquents from arrested cases of dementia precox. In the latter can usually be observed evidences of characteristic mannerisms, stereotypies, and emotional apathy, as well as remnants of a higher grade of

intelligence. In differentiating complete idiocy from advanced dementia it may be noted that the rhythmic movements of idiots which simulate stereotypies and mannerisms are easily interrupted by outside influences, while the attention of the dement is indistractable and his behavior little influenced by his environment.

**ETIOLOGY.**—Although the actual cause of dementia precox is not clearly understood, there are many points of interest and of significance in this connection. While the disease is not usually directly hereditary, the family histories of the patients usually disclose neuropathic taints, such as insanity of different forms, hysteria, alcoholism, etc., in the parents or near relatives, and two or more cases of dementia precox frequently occur in the same family. Physical stigmata of degeneration occur more commonly on these patients than in normal individuals, and many of them present mental eccentricities or even precocious ability from early youth. Thus it would appear that, although the disease cannot be classed as directly hereditary, a congenital predisposition exists which is largely dependent upon hereditary influences. This predisposition is manifested in a lack of resistance and of recuperative force of the nervous system, explaining the precipitation of the disease by various causes, such as mental and physical shocks, worry, exhausting fevers, confinements, hemorrhages, etc.

The view of Régis that dementia precox is essentially an intoxication is widely held, and has much evidence to support it. The accompanying physical conditions, including deranged metabolism and diminished

resistance to infections, suggest perversions of the functions of the ductless glands. The facts that the disease develops almost exclusively during the years of sexual activity, and that the sexual functions are frequently deranged, indicate that disturbances of the internal secretions of the sexual glands may be a factor in the etiology of dementia precox.

The theory that the disease may develop upon an exclusively psychogenic basis, as Jung and others are inclined to believe, is not widely accepted and seems improbable, as the physical symptoms, the course of the disease, the terminal dementia which occurs in the great majority of the cases, as well as the pathological evidence so far revealed, indicate very strongly a physical basis for the mental symptoms.

Existent evidence for the organic nature of dementia precox is not wholly convincing, since similar cytological changes are found also in cases of toxic deliria and in cases complicated by severe venereal disease, while the stratigraphical changes described are found also in certain senile cases without characteristic symptoms of dementia precox. Resort must, therefore, be had to the topographical idea, for the adequate exploitation of which total brain sections, with cytological exploration of all areas, are necessary.

As regards the curability of dementia precox the remissive character of some cases, the speedy disappearance of particular symptoms, the persistent complexity of reaction in some instances, the absence of characteristic severe projection system symptoms, all indicate that the process is histopathologically mild, and that the focal changes found will be but slightly destructive or even irritative. Southard (Boston Med. and Surg. Jour., Aug. 4, 1910).

Chemical studies have shown the existence of a peculiar change in the chemical composition of the brain, consisting of a deficiency in the metabolic or chemical activities of the nervous system, the exact interpretation of which is at present impossible. The foundation for the deficiency here met with lies, probably, in some disturbance occurring during early or embryonic development, as a result of which the brain fails to acquire its full metabolic activity and recuperative power. Such a nervous system can meet simple conditions, but when subjected to the strain of adolescent life it gradually deteriorates, producing the chemical differences observed. This view supplies a chemical or metabolic basis for the idea expressed by Kraepelin, and in a manner supplements the anatomical view elaborated by Bolton, namely, that deterioration of the nervous system cannot take place unless there is an underlying instability of the neurone. The writer has made chemical observations with sulphur, and finds that the chemical analysis of brains from cases of dementia precox reveals a variation in the neutral sulphur fraction; in other words, a difference in chemical composition of a nature not so far observed in other forms of insanity, or in cases free from mental disease. Because of the chemical relationship of this group of sulphur compounds to a similar group in the urine, and in view of the suggestion of Folin that in the urine this group may bear some relation to tissue metabolism, he concludes that in dementia precox there exists a condition of metabolic deficiency. He believes that the absence of demonstrable macroscopic or microscopic anatomical changes in the brain of these cases gives to this chemical finding an especial significance. W. Koch (*Jour. of Exper. Med.*, March, 1911).

Examination of the heart showed the cardiac area to be but slightly diminished. The apex beat was hardly visible or palpable. Mur-

murs were audible in 25 per cent. The medium-sized and small arteries showed a certain thinness of their walls and a feeble pulsation. Cyanosis of the face and extremities and diminished visibility of the superficial veins were frequently observed, as also the phenomenon of dermatography. The axillary temperature was always within physiological limits, but it was noteworthy that in the majority of cases the temperature on the left side was one or two decimals of centigrade above that on the right. The writers conclude that the subjects of dementia precox do not present grave anatomical or functional disturbances sufficient to differentiate them clearly from the normal, though they certainly present features indicative of a deficiency and torpidity of the circulatory function. L. Lugiato and G. B. Lavizarri (*Riv. Sper. di Fren.*, vol. xxxvii, Fasc. 3, 1911).

In a study of 17 cases in which a connection between the mental disease and tuberculosis was so close that certain writers have considered the one as due to the other. This again opens the question as to the possibility of splitting the great dementia precox group into two main groups on the physical side: those of toxic-infectious nature, often tuberculous, and the true degenerative psychosis. This grouping has nothing to do with the mental groupings. H. I. Gosline (*Jour. Lab. and Clin. Med.*, Apr., 1919).

**PATHOLOGY.**—Although definite and constant pathological findings in dementia precox have not been reported, there is some evidence that actual changes exist in the nervous system which are responsible for many of the psychic and physical symptoms of the disease. Many different investigators have found various changes in the brain-tissues from cases of dementia precox. Southard (1910) has found abnormal neuroglia growth or sclerosis in the cortex. Alzheimer and others

have recorded cases in which the cortical cells were diseased, their number reduced, and products of degeneration present in the brain-tissue. W. Koch (1911), who from chemical investigations determined a deficiency of certain constituents of the brain-tissue, especially of the sulphur compounds, thinks that this deficiency is acquired early or may even be congenital, and that it is associated with lowered metabolic and chemical activities; reduction in the vitality, resistance, and recuperative ability of the individual, predisposing to early degeneration or breakdown. The very frequent occurrence of tuberculosis and other infections in patients suffering from dementia precox is evidence of their diminished resistance, but it also renders difficult the interpretation of pathological findings, since these may be at least in part dependent upon the complicating condition.

**TREATMENT.**—Since certain tendencies are often recognizable in many individuals predisposed to dementia precox, the importance of measures instituted to counteract these tendencies can readily be appreciated. Nervous instability, eccentricities in character, and the "shut-in" type of personality often noticeable in childhood are indications for special consideration in matters of education and personal hygiene. The personality of each individual should be carefully studied, and efforts directed to the correction of any defects in character by education and training. Knowledge of sex physiology and hygiene should be appropriately imparted, and stresses or excesses of all kinds should be carefully guarded against. The frequent precipitation of dementia precox in those who are suddenly forced to face entirely new conditions, as in the case of

immigrants or pioneers, and their improvement upon return to former conditions emphasize the necessity for a protected, rational life for those in whom limitations in adaptability are apparent.

On the basis of Kraepelin's opinion expressed some years ago that dementia precox was best explained by a toxemia which entailed deterioration and destruction of the cortical cells, and his experimental observation that saline solution caused an increased feeling of hunger and thirst accompanied by improvement of general health, its clinical use has been introduced by Ishida, of Nagasaki, Japan. Improvement having been observed in most instances, the use of the solution is now being tried by various authors.

Kraepelin having ascertained experimentally that sodium chloride infusions caused "an increased feeling of hunger and thirst accompanied by a regular improvement of the general health," the writer tried their use in dementia precox, using a 0.9 per cent. solution intravenously where possible, in quantities ranging from 300 to 1000 grams, repeated where this was done on an average of four cases about every 12 days, 2 or 3 times. In 1 case there was no change excepting a temporary increase of interest; in 3 there was lasting improvement; in 4, remissions lasting from 1 to 3½ months; in 1, a remission which may have been spontaneous; in 1, sufficient improvement to warrant discharge. N. Ishida (*Amer. Jour. of Insan.*, vol. 73, p. 542, 1916-17).

In a total of 15 cases treated with saline infusion by the writer, the results were as follows: 10 cases, very unclean before treatment, were improved in this respect. In 8 cases, there was an awakening in interest in work, directly following the treatment, and in 7 of these cases, this has continued. Remissions occurred in 6 of the 15 cases but these improved again on reinjection of the solution; 7 cases have greatly im-

proved without remission. One apparent cure, without remission since treatment was commenced 5½ months ago. Second apparent cure without remission for 3 months. This case has put on 25 pounds in weight and improved mentally to a surprising degree. All 15 cases showed increase in appetite for food and all gained flesh. L. V. Guthrie (W. Va. Med. Jour., Dec., 1917).

In 10 cases of dementia precox the writer administered intravenous injections of 0.9 per cent. salt solution made in freshly distilled water, by the gravity method. The initial dose was 3 c.c. per kilogram of body weight. Each succeeding dose was increased by 30 c.c. (1 ounce) and injections were made at 7-day intervals for a period of 4½ months. Seven of the 10 patients showed no mental improvement; of the remaining 3, 2 brightened up slightly, the third brightening up enough to work. Eight of the 10 patients gained in weight from 2 to 15 pounds; 1 patient lost 1 pound and 1 patient remained stationary. Miller (Arch. of Neurol. Psychiat., Mar., 1919).

The favorable results are accounted for by combining Kraepelin's view that dementia precox is best explained by an autointoxication leading to deterioration and destruction of the cortical cells with Sajous's view (1903) that the cerebral neurones receive blood plasma through their neurofibrils, thus insuring the penetration of toxins to the neuron itself, which toxins cause the lesions in the cortical neurons, recognized post mortem. The toxins are, at least in some cases, known to be derived from the cecum owing to fecal stasis therein.

The theory, to be brief, is as follows: Dementia precox as clinically recognized is a symptom complex, due in the main to a toxemia. The toxin acts upon the brain to produce the lesions recognized at autopsy, and the mental disturbances and ultimate deterioration recognized during life. The toxin is produced in the cecum by the growth of micro-organisms (of the colon group) upon the unas-

similated portion of the food protein, or upon the excreted waste protein entering the ileocecal valve (especially the histidin) on account of a protracted cecal stasis (or in other cases on account of an incompetency of the liver to destroy iminazol-containing toxins in the portal circulation). The cecal stasis is due to a spasm of the ring of Cannon, which spasm itself may be due to a general spasmophilia from calcium poverty of the blood and lymph or to other undetermined causes. Research Laboratory of Psychopathic Hosp., Cook Co. Hosp., Chicago (Dementia Precox Studies, July, 1918).

All the glands of internal secretion are abnormally stimulated, the purpose being, according to Sajous in so far as the thyroid, adrenals and pancreas are concerned, to enhance the antitoxic powers of the blood, while others again, the thymus, for instance, as a result of the stimulation, replace nucleins which supply the brain cells with their main components.

That the internal secretions play a rôle is probable. Sajous has pointed out the cogent facts indicating an important rôle played by the thymus gland. In keeping with the view he presents are not only the facts pointing to a defective nervous development, but also the observations of Barbo and Habderkandl of the occurrence of osteomalacia in dementia precox. Various facts point to other structures as well. Occasionally the thyroid gland is enlarged; more frequently small. Thus in 7 autopsies 5 thyroids were little more than ½ the normal weight, 1 was ¾, and 1 was approximately normal. Out of 8 pairs of adrenal glands, 5 were greatly in excess, 1 decidedly below normal, and 2 about normal. The most constant finding in the adrenal picture was the small amount of fat in the cells of the cortex. Clinically his attention has been strongly attracted to the sex glands, the anomalies of menstruation, the delayed and imperfect establishment of puberty on the one hand, or of sex-

ual precocity on the other. Again, there was a history of sexual excesses, sexual vagaries, and perversions. A relation to the sex glands is further indicated in the accentuation of the symptoms often observed during the menstrual epoch and by the occasional incidence in a pregnancy, in repeated pregnancies, or in a miscarriage, as though sex exhaustion played a rôle. F. X. Dercum (Trans. Amer. Congr. Internal Med.; Med. Rec., Jan. 20, 1917).

Excessive stimulation and the resulting hyperemia of these various organs eventually lead to atrophy. In case of the sex glands, this is apt to occur early, the testicle and ovaries undergoing atrophy.

In the majority of the cases of dementia precox, especially in the hebephrenic type, the Abderhalden reaction showed that there is an imperfect functioning of the reproductive organs, and in the catatonic excitement stage of the thyroid. A. Fauser (Deut. med. Woch., Feb. 13, 1913).

The writer found microscopic changes in the brain in dementia precox which he attributes to abnormal functioning of certain ductless glands, especially the thyroid and genital glands. Frankhauser (Correspondenzbl. f. schweizer Aerzte, Jan. 17, 1914).

The writer observed that the pathologic findings in dementia precox seem identical with those found in animals after partial destruction or total removal of the thymus. Attempts to treat animals and human beings with thymus extract or in substance gave no results. Transplantation of thymus tissue is advised, although Klose and Vogt have reported eventual absorption in 2 dogs in which scraps of thymus tissue had been implanted in the omentum and spleen, both animals having been thymectomized. Ebbell (Norsk Mag. f. Laegen., Dec., 1914).

In a study of the Abderhalden tests in 289 cases by the writers, the findings in dementia precox were positive to sex gland in 46 out of 58

cases tested, or 81 per cent., and in 9 cases negative. Blood-counts in dementia precox gave wide deviations from the normal. The leucocytes were low, in one case 2100 per c.c., and averaging about 6500. Coupled with this was usually a slightly increased pulse rate with low blood-pressure and subnormal temperature. Notable was the fact that 75 per cent. died of tuberculosis. Cotton, White and Stevenson (Jour. Nerv. and Mental Dis., Feb., 1917).

The treatment of dementia precox on these modern lines, therefore, resumes itself at the present writing (1919) in eliminating as far as possible, the cause of the toxemia. In most instances this is due to cecal stasis, ascertained by means of X-ray and a barium meal. The latter may indicate retention of fecal contents from two days to three weeks, the toxemia being due to absorption of toxins, derived from catabolized products of histamin attributed to a special type of bacillus coli. Besides the **saline solution intravenous infusions** referred to above, attempts should be made by large **saline solution enemas** at 108° F., to flush the colon and perhaps the cecum by causing the patient to lie on his right side immediately after the enema. By this means the writer (Sajous) has obtained cessation of the fecal impaction and considerable improvement. If the case fails to improve materially then **appendicostomy** or **cecostomy** is indicated to permit the daily flushing of the colon through the opening in the abdominal wall with saline solution.

Remarkable improvement and even recovery in a few patients treated by **appendicostomy** and protracted irrigation of the cecum and colon with large quantities of water. By this direct and positive method the attempt has been made to arrest the production of toxic amines in the cecum, and diminish the amount of toxic substances absorbed. Dementia precox is a progressive disease. While there are distinct clinical remissions, there are few permanent recoveries. It is generally considered a condition hopeless of recovery

even with defect. Research Laboratory of Psychopathic Hosp., Cook Co. Hosp., Chicago (Dementia Precox Studies, July, 1918).

When these measures are carried out early in the history of the case before the cortical cells have undergone incurable deterioration, **thymus gland** is of value to supply the cortical cells the nucleins required for the elaboration of their functional constituents, while small doses of **thyroid gland** will serve to sustain their metabolic activity. EDITORS.

The writer found that the administration of very small doses of **thyroid extract**, alternated with an alcoholic solution of **lecithin**, induced decided effect in very early cases of the malady, and 3 cures resulted. H. J. Berkley (Monthly Cyclo. of Pract. Med., Apr., 1908).

When dementia precox develops during puberty the thyroid gland is deficient in many cases. He found that it subsided under thyroid treatment in 11 of the 12 cases, men 17 to 24, the others girls of 19 to 21. The improvement in 8 was striking. Lemel (Nederlandsch Tijds. v. Geneesk., July 25, 1914).

The writers recognize 2 clinical groups of dementia precox, one attended with a low blood-pressure and a negative Abderhalden reaction to testicle and pancreas, the other positive Abderhalden reaction and a high blood-pressure. They then administered **thymus extract** in cases showing high blood-pressure and giving the Abderhalden reaction. Out of 6 cases, 3 gave excellent results, the patients being well at the time of publication. Ludlum and White (Amer. Jour. of Insanity, Apr., 1915).

The treatment of the active manifestations of the disease is necessarily symptomatic, and the average case is best handled in an institution. In the states of excitement the most efficacious measure is the prolonged **warm bath**, which generally renders sedative drugs unnecessary; in violent excite-

ment, however, medication may also be indicated and **hyoscine** (gr.  $\frac{1}{100}$ —0.0006 Gm.) alone or with **morphine** (gr.  $\frac{1}{4}$ —0.016 Gm.) may be given hypodermically and repeated at two-hour intervals until effective. In catatonic stupor **forced feeding**, **enemata**, and **catheterization** are often imperative. In the stuporous as in the excited states the prolonged **warm bath** is of great value. Attention to proper elimination is also important. **Thyroid gland** alternating with small doses of **lecithin** have proven of value in certain cases during the early stages of the disease.

It is absolutely necessary that patients in the active stages of dementia precox should be under careful supervision in view of their pronounced tendency toward suicide and violence, making them a source of danger to themselves and those about them. The catatonic acting on blind impulse and the paranoid on his secret delusions are among the most dangerous of lunatics.

During the quiescent states and the intermissions attention should be directed toward the rational management and training of the individual case. Employment within the capacity of the patient, systematic and regular habits, outdoor exercise, and protection from the complexities of life and all enervating influences are fundamental requirements.

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## DENGUE. — DEFINITION.—

An acute, highly infectious, non-contagious disease of the tropics and subtropics, characterized by paroxysmal fever, severe pain in the joints and muscles, multiiform and irregular rashes, tendency to relapse, and low mortality.



**SYNONYMS.**—Dandy fever, from the stiff limbs and awkward gait, the Spanish word *dengue* having an allied meaning; break-bone fever, sun fever, solar fever, broken-wing fever, three-day fever, bouquet or bucket fever, eruptive articular fever, eruptive rheumatic fever, dingee, denguis.

**HISTORY AND DISTRIBUTION.**—The disease was first recognized in Spain in 1764 to 1768. An outbreak in 1779 in Cairo and Java was described by Brylon, and the epidemic in Philadelphia of 1780, by Dr. Rush. In 1824 it prevailed in India, and in 1827 and 1828 in the West Indies, and in the cities of Charleston (where the late Dr. S. H. Dickson lived and described the disease), Savannah, and New Orleans in the United States. Since 1828 there have been several extensive epidemics in the tropics and in the Gulf States, the last occurring in 1897. In 1888 the disease extended as far north as Virginia, but, so far as known, it has not occurred north of New York and Boston, where a few cases have been recognized. In the summer of 1907 dengue prevailed at Brownsville, Texas, 1000 cases, out of a population of 8000, occurring between the middle of June and the middle of August. Reports of this epidemic were made by Joseph Goldberger and George W. McCoy, of the Public Health and Marine Hospital Service, who think that the disease was introduced from Mexico across the Rio Grande. More recently epidemics have occurred in Australasia (1911) and in our own country, in Beaufort County, S. C., where, according to C. H. Halliday (Military Surgeon, August, 1911), it has existed from time immemorial.

Characteristic of dengue are the suddenness with which it affects a com-

munity, the rapidity of its diffusion, and its pandemic feature. Within two months 20,000 persons were attacked in the epidemic of 1897 in Galveston, Texas. It follows lines of travel, is carried by infected persons, and is arrested by cold weather. High altitudes are unfavorable to its spread.

**SYMPTOMS.**—There are no prodromata, the onset of the disease being sudden, and attended with chilliness, lassitude, headache, backache, anorexia, coated tongue, and intense pain in the muscles and joints. The respirations are quickened, and the pulse usually, though not invariably rapid in proportion to the temperature. The urine is scant, high-colored, concentrated, and at times albuminous. The temperature rises rapidly and may reach 106° or 107° F. in several hours. The face is congested and bloated, the conjunctivæ injected, and the mucous membranes flushed. The superficial lymph-glands are enlarged and often red, and the testicles may be involved. Mild delirium, nausea, and vomiting may occur. The joints are painful, tender, and at times swollen. In the early stages of the disease there is an erythematous rash.

In from one to three days a crisis occurs, with subsidence of the fever, free diuresis and diaphoresis, and, in some cases, diarrhea and epistaxis. In some cases the fever ends by lysis. The headache and constitutional symptoms abate, but weakness and a certain amount of joint-pain and stiffness remain. The remission, lasting from two to five days, is followed by a return of the fever, and, to a greater or less extent, of the other symptoms. During the remission, or with the onset of the second febrile paroxysm, a rash appears, which is irregularly distributed, and may be roseolous, macular, papular, or even

vesicular in character. It is usually seen first on the hands, and spreads over the entire body, and may resemble that of measles, scarlet fever, or urticaria. Desquamation often occurs and may persist for several weeks. It is frequently slight and very fine. The eruption occurs in about one-half of the cases. Abortion is rare. The duration of the disease is from seven to ten days.

During the dengue epidemic of 1902 and 1904 in Beyrouth, Syria, the symptoms varied. In one epidemic there were eruptions in nearly every case; in another, no cutaneous manifestations. In 1 case the disease was very mild; in others it would simulate severe typhus. In a recent epidemic 26 cases developed in eleven days; the onset was sudden and severe, the fever reaching its maximum, 104° F. (40° C.), or thereabouts, suddenly, and dropping to below normal on the third day. A painfulness of the ocular muscles seemed to be pathognomonic. In another epidemic the fever was about 104° F. (40° C.) for thirteen days, then dropped abruptly. De Brun (*Revue de méd.*, vol. xxvi, No. 6, 1906).

In but few acute diseases is the symptom complex of adrenal insufficiency so frequently—in fact, almost regularly—encountered as in dengue: Profound asthenia, sometimes sudden in onset, but almost constant; lumbar and especially epigastric pain and tenderness, and vomiting, sometimes incessant, together with fever and various neuralgic pains, may be cited as the fundamental symptoms of the disease. Of 7 cases studied in Syria in 1912, all gave, with great clearness, the "white line" phenomenon of Sergent. Three rapidly improved under 30 drops of a 1:1000 solution of *adrenalin* by the mouth, and the white line could no longer be elicited thereafter. Khoury (*Bull. et mém. de la Soc. méd. des Hôp. de Paris*, Nov. 13, 1913).

\* The blood examination in dengue has recently been receiving merited atten-

tion, and valuable contributions to the subject have been made. Owing to unavoidable circumstances no erythrocyte or leucocyte count was possible at Brownsville; but Edward B. Vedder (U. S. A., Manila) has reported the blood conditions in 20 of the cases occurring among the troops at Fort William McKinley. He states that his findings are practically in accord with those of Carpenter, Sutton, and Stitt. All of these observers agree that nothing of importance attaches to the red cells. The differential leucocyte count reveals a constant leucopenia, early and marked reduction of the polymorphonuclear cells, increase of small lymphocytes, gradual, but much more moderate increase of large lymphocytes, and gradual, but slight increase of eosinophiles.

Dengue is one of the few fevers in which a leucopenia persists from the first. It is suggested that the causative agent is a small diplococcus or a delicate bipolar staining bacillus closely resembling Pfeiffer's organism. It is probably transmitted by the respiratory tract, and its virulence is much increased by the presence of the essential meteorologic factors and by overcrowding. Carpenter and Sutton (*Jour. Amer. Med. Assoc.*, Jan. 21, 1905).

Leucopenia is a constant feature of dengue; there is also a marked reduction in the polymorphonuclear count early in the disease. Coincident with this decrease in polymorphonuclears is an increase in the small lymphocytes and a gradual, though much more moderate, increase in the large lymphocytes. There is a similar gradual but slight increase in the eosinophiles. Vedder (*N. Y. Med. Jour.*, Aug. 3, 1907).

Among the uncommon symptoms are marked pain in the eyes, which occurs early in the disease; jaundice, black vomit, hematuria, and active delirium.

Cutaneous hyperesthesia is sometimes observed and may linger for a month. The appetite may be good during the entire attack. One case is recorded with intestinal hemorrhage lasting three months and terminating in death.

The second paroxysm is usually shorter and milder than the first, and, in the majority of cases, is succeeded by rapid convalescence; but soreness and stiffness of the muscles and joints, physical and mental debility, insomnia, boils, or other conditions may reduce the patient's strength and retard his recovery. A third febrile paroxysm is exceptional, but relapses are not uncommon, and may occur at the end of two weeks. There are a certain number of atypical cases, some with slight fever and marked eruption, others with high fever and practically no eruption.

**COMPLICATIONS AND SEQUELÆ.**—Insomnia is common. Convulsions have been known to occur in children. Hyperpyrexia, pericarditis, meningitis, and muscular atrophy are very infrequent. The respiratory and gastrointestinal mucosa may be the seat of severe catarrhal inflammation. Among the sequelæ occasionally noted are chronic urticaria, asthma, pleurisy, chorea, peripheral neuritis, transient dementia, and lingering vertigo.

**DIAGNOSIS.**—Dengue is distinguished from influenza by the catarrhal symptoms of the latter disease, the absence of secondary or tertiary paroxysms, and the detection of the specific microbe; but the differentiation may not be easy should epidemic influenza be prevailing, assuming the nervous type, or showing, as it occasionally does, a cutaneous rash or herpes. In malaria the detection of the plasmodium, enlargement of the spleen, periodicity of the paroxysms, and effect of quinine

determine its nature. Acute rheumatism is known by its irregular fever, pronounced inflammation of the joints, and continuance; scarlet fever by the sore throat, vomiting, continuous fever, and early appearance on the chest of the characteristic rash; röteln by the symptoms of invasion, the absence of lymphatic enlargement, and the primary location of the eruption, and syphilitic roseola by the history of the case, usual absence of marked fever, and distinctive glandular involvement. The differentiation from yellow fever is of great importance, inasmuch as both diseases have been known to prevail at the same time. In yellow fever the joint symptoms are less pronounced, and are of shorter duration; the facies is different, jaundice appears early, the pulse is disproportionate to the elevation of temperature, black vomit is more constant, and renal symptoms, with marked albuminuria, are pronounced. In the Brownsville epidemic yellow fever was excluded by the eruption of dengue and the absence of albuminuria and jaundice, while Faget's sign, a falling pulse with stationary or rising temperature, was not seen in a single case. The blood-count promises to be of decided value in distinguishing dengue from malaria and yellow fever. The former disease would be indicated by slight leucocytosis and marked increase of large mononuclear and transitional cells; the latter by a normal or increased number of leucocytes, normal number of polymorphonuclear cells and small lymphocytes, and scarcity of eosinophiles. At the same time the blood test is not infallible in dengue. In order to obtain the best results, examinations should be made early and be repeated, the information obtained being available on the second or third day of the disease. M.

L. Graves calls attention to the following observations made upon 8 cases of dengue occurring during the epidemic in Galveston in 1908: The true Faget pulse was not found, but a pulse rate disproportionately slow to the elevation of temperature; the presence in 5 of these cases of a positive diazo reaction, whereas Corput states that in 2000 examinations of urine in yellow fever the reaction was never present, and a marked leucopenia, with no significant changes in the red cells or the hemoglobin. On the other hand, Vargas and Seidelin (May, 1909) report a positive diazo reaction in 9 out of 22 cases of yellow fever. They do not attach much importance to the diagnostic or prognostic value of the reaction. In the discussion of Graves's paper strong evidence was adduced to prove that dengue could be prevented by the use of mosquito lotions and bars.

During the epidemic of dengue which occurred in Havana in the fall of 1905, great difficulty was encountered in the diagnosis of the disease, especially during the first forty-eight or seventy-two hours, when it could readily be mistaken for yellow fever. Agramonte (N. Y. Med. Jour., Aug. 4, 1906).

In the epidemic of dengue as it occurred in Brownsville, Texas, during the summer of 1907, a number of patients gave histories of previous attacks, and at least 2 had had yellow fever. The disease corresponded closely with that observed in the Philippines, but there hemorrhages were not observed and enlargement of the lymphatics was more common. The diagnosis in the presence of an epidemic was not doubtful. Yellow fever, the only disease demanding serious consideration, was readily excluded by the eruption and the absence of albuminuria and jaundice, which would certainly have been present with the fever of such sever-

ity and duration. J. Goldberger and G. W. McCoy (Jour. Amer. Med. Assoc., Dec. 7, 1907).

**ETIOLOGY.**—Dengue is favored by warm weather and, to a limited extent, by faulty hygienic conditions. It has been claimed that, as a rule, immunity is conferred by one attack, but the reports of recent outbreaks of the disease prove that a number of cases had been previously affected. No race, age, or sex is exempt. McLaughlin, of Texas, has described a micrococcus which he claims to be the specific cause, while H. Graham, of Beyrout, Syria, called attention in 1903 to an organism resembling the malarial plasmodium and supposed to be transmitted through the *Culex fatigans* or other species of mosquito.

Beyrout, Syria, offers peculiar advantages for the study of the mode of propagation and the pathology of dengue. It is very prevalent while the city is infested with mosquitoes, among which only certain forms of culex are found. Most of all villages on the mountain-side contain a certain number of mosquitoes, which are also only the culex, though some of the villages in the dryer part have none. The writer conducted studies with the aim of determining whether the culex could carry dengue from person to person. He found that the disease did not appear when persons under observation were not bitten by infected mosquitoes, but that it did appear invariably when they were so bitten. He became convinced that the mosquito was the means of carrying the disease, and this led him to a careful examination of the blood in over 100 cases; in all of these he found ameboid organisms in the red blood-cells. They closely resembled the *Plasmodium malariae*, differing from this, however, in the cycle of production, or formation, in the human blood in that in dengue it takes much longer. The changes in

the life phase come more slowly and are more difficult to follow. Flagellate bodies were also encountered. The constant presence in the red blood-cell of the hematozoön during the fever, its resemblance to the parasite of Texas cattle fever, its likeness in manner of growth and mode of propagation by the mosquito to the malarial parasite, all lead the writer to conclude that in this parasite he has discovered the cause of dengue. Harris Graham (Med. Record, Feb. 8, 1902).

Ashburn and Craig (1907), stating that they have produced typical attacks of dengue in healthy men by intravenous injection of filtered and unfiltered dengue blood, conclude that the cause of the disease is ultramicroscopic in size, and that the most common mode of transmission is through the *Culex fatigans*. Ross, writing in July, 1908, states that the extermination of mosquitoes in Port Said has caused not only malaria, but also dengue, which was very prevalent, to disappear, and believes that the disease will cease with the extinction of the mosquito. A. H. Allen (U. S. N., Cuba, Aug., 1907), reporting a mild and limited outbreak in two companies of United States Marines at Lajas and Santo Domingo, forty miles from the sea coast, refers to the abundance of mosquitoes during the entire year. The most frequent species were the stegomyia, culicidæ, and anopheles, in the order named, and the measures adopted to kill them and screen the patients appeared to check the spread of the disease and confirm the present view as to the mode of transmission. Megaw considers it probable that the seven-day and three-day fevers of India, described respectively by Rogers and McCarrison, are identical with dengue, while Leonard Rogers, inclining to the belief that seven-day fever

and dengue are not the same, gives the points of resemblance and difference in the two diseases.

In an epidemic of dengue which suddenly made its appearance among the Americans who had been on St. Thomas Island 3 to 8 months, the important feature was the agent carrying the infection. The *Stegomyia calopus* is practically the only mosquito seen and inhabiting the localities where the disease was most prevalent, and the only place where the mosquito bite seemed to do any damage. The mild character of the bone pains was characteristic. Involvement of the lymph glands, in many cases, was quite severe. No breaking down or suppuration subsequently has been noted. The epidemic gradually faded out. With the decrease in rainfall it had almost disappeared. Only an occasional individual who had just arrived would become infected. During the dry season when mosquitoes were very few, dengue was practically absent. Lane (U. S. Naval Med. Bull., Oct., 1918).

Epidemics of dengue have been known to die out in Costa Rica when mosquitoes were excluded from the homes affected. The disease is not known in the mountains. Figueroa (Bol. de la Asoc. Med. Porto Rico, June, 1918).

Microscopic studies of the blood in the cases at Manila, July, 1905, failed to reveal a specific microbe. The *Stegomyia calopus* and *Culex pipiens* were abundant at Brownsville; but the observers state that no causative microorganism was found. The conclusion, based upon the foregoing reports and investigations, is that the mosquito is probably the intermediary host and infecting agent, but that the specific microbe is yet undiscovered.

During the latter part of the year 1907 dengue became epidemic in certain parts of the Philippine Islands. During the wet weather period

mosquitoes were very troublesome, and, although the post was well policed and there was no standing water, the insects were present in large numbers. The barracks of the 19th Company were situated on the highest point of the post, seemingly an unfavorable situation for the presence of mosquitoes, while the barracks of the 14th Company were somewhat lower down and some distance away.

In attempting to control the epidemic the sanitary precautions employed were as follows: All men in barracks were required to keep their mosquito bars around them at all times. There being no hospital at the post, all sick had to be treated in their quarters; these were screened with especial care, inspections being made at stated intervals four or five times a day to see that directions were followed. In addition it was recommended to the commanding officer of the garrison that the pass list to visit the barrio at night be suspended; this recommendation was also followed.

Out of the 8 white residents of the post, no one contracted dengue, but a soldier who occupied a small room in the house of the commanding officer was taken sick. This man had slept without any mosquito bar, and it is a significant fact that a second soldier, who occupied a bed alongside of the first, and who habitually slept with his mosquito bar down, escaped. H. W. Jones (Boston Med. and Surg. Jour., Jan. 14, 1909).

The careful consideration of all the facts impresses one with the belief that yellow fever, dengue, and papataci fever, as well as other diseases due to a filterable virus, are caused by parasites which differ markedly from any with which we are acquainted. The evidence goes to show that they differ from one another in virulence, thus producing the variations in the clinical pictures of the three diseases, just as in malarial infection we have different species of plasmodia, which produce mild or

severe attacks. In many respects these fevers resemble those due to the malarial plasmodia. Craig (N. Y. Med. Jour., Feb. 25, 1912).

Dengue fever is caused by a parasite very closely related to that of yellow fever, a spirochete, *Leptospira icteroides*. The writer, therefore, advocates the search for a similar organism in the blood of dengue patients, using cultural and animal experimentation methods followed by Noguchi in his demonstration of *Leptospira icteroides*. In 1906, Ashburn and the writer believed this disease might be caused by a spirochete, and in their work they used every method available at that time to find such an organism in the blood of dengue patients, but without success. The anerobic culture methods devised by Noguchi, so successful in cultivating spirochetes, and improved methods in animal experimentation are powerful aids which, if properly applied in the study of the etiology of dengue fever, would lead to the discovery of the causative parasite. C. F. Craig (Jour. Amer. Med. Assoc., Oct. 30, 1920).

**PATHOLOGY.**—The disease being rarely fatal, no observations on the morbid anatomy have been recorded.

**PROGNOSIS.**—This is favorable, and the few deaths reported have been due either to an unusually severe attack, to complications, or to an association with other diseases. Aged persons and young children are more prone to ill consequences, and may be predisposed by dengue to the invasion of more serious maladies. Death from syncope has occurred in several instances at the crisis.

**TREATMENT.**—There is no specific treatment, and the hygienic measures employed in the infectious diseases are applicable. **Rest in bed, light or liquid food, cholagogues or other purgatives as needed, pure water freely, and sleep will promote the patient's**

welfare and comfort, and tend to shorten the course of the disease. The fever can be reduced by **hydrotherapy** and sudorifics, such as **spirit of nitrous ether**, **neutral mixture**, and solution of **ammonium acetate**, to which, in mild cases, the **bromides** can be added to allay the nervous symptoms and secure sleep. The **coal-tar** and **salicylic acid compounds**, judiciously administered, will also lower the temperature as well as mitigate the pains. When the suffering is intense, the subcutaneous use of **morphine** or **codeine** will be required. The wakefulness sometimes produced by these drugs can be counteracted by **sulphonal** or one of its allied products. Tincture of **belladonna** and tincture of **gelsemium** may prove serviceable. The joint pains can be combated, especially when swelling and redness exist, by **hot fomentations**, **anodyne liniments**, or other local measures used in rheumatic arthritis. Cephalalgia may yield to an **ice-bag on the head** and a **hot mustard foot-bath**.

In the more severe cases active medication suited to the symptoms is needed. Threatened convulsions call for rectal injections of **chloral hydrate** and the **bromides**. Precaution should be taken against collapse in children and feeble subjects. **Iodide of potassium** has been recommended for the continued joint-pains of convalescence. **Quinine** is said to be a preventive, but its value is, not established.

The convalescence of the patient always demands close attention, in order that complications may be avoided and relapses prevented. **Tonics** and **hematics** are indicated in persistent weakness. When the patient is left

unrecuperative and debilitated, recovery will be hastened by removal to the **seashore** or **mountains**.

In the epidemic which occurred recently in Beaufort County, S. C., the writer pursued the following plan of treatment in all cases: Patients put to bed and given a cathartic, usually 30 c.c. (1 ounce) **oleum ricini**. The diet consisted of milk and broths at two-hour intervals, until the temperature declined to normal.

Pain was the symptom most complained of. In the milder cases, **phenacetin**, **acetanilide**, and **caffeine citrate** in combination controlled the pain. In the severer cases, **morphine** was required. It was given in 8-mg. ( $\frac{1}{8}$  grain) doses, hypodermically, and repeated in two hours if necessary. More than the second injection was never required. For the intense headache an **ice-cap** brought grateful relief. A **cold sponge-bath** was employed to reduce the temperature, and at the same time served to diminish the restlessness.

In some cases **quinine** was given at the onset, while in others it was withheld until the disease was well established. From his own observations, the writer is of the opinion that the judicious use of quinine at the onset will serve to shorten the course of the disease, while in those cases which are well established the drug has no specific action. During convalescence a general **tonic** was given.

"Low-country fever," or dengue, which existed in Beaufort County, S. C., during the fall of 1910, in epidemic form, will continue to exist in sporadic and epidemic form until the inhabitants realize the necessity of providing themselves with protection from the bites of mosquitoes. Chas. H. Halliday (Military Surgeon, Aug., 1911).

WILLIAM S. GORDON,  
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**DERCUM'S DISEASE.** See  
ADIPOSIS DOLOROSA.

**DERMATITIS.**—Dermatitis signifies merely inflammation of the skin. Such inflammations may occur from a great variety of causes; indeed, all of the inflammatory diseases of the skin are, in a sense, a form of dermatitis. The term as here used, however, is restricted to acute inflammations, the result of known irritants. This will exclude from consideration such affections as dermatitis herpetiformis, a disease closely allied to pemphigus; dermatitis gangrenosa, a condition commonly resulting from obstruction of blood-vessels, and certain other dermatoses to which the term dermatitis is prefixed and which are described under the next general heading.

Dermatitis herpetiformis, erythema multiforme, urticaria, pemphigus, and some other bullous affections of uncertain classification are toxemias due to a great variety of toxic substances which may be introduced into the body from without, may arise from autointoxication, or from local or general bacterial infection; and although they differ from one another sufficiently in their symptomatology and course to entitle them to be considered as separate and distinct affections, are essentially one in their pathogenesis. Hartzell (Jour. Cutan. Dis., March, 1912).

The description of dermatitis under the present head will, therefore, be circumscribed to a consideration of various inflammations of the skin resulting from external irritants, in addition to those which are due to the ingestion of certain drugs.

All forms of dermatitis of external origin are due either to the action of traumatism, heat or cold, or chemical irritants. For purposes of classification and study the following varieties are, therefore, distinguished:—

(a) Dermatitis traumatica.

(b) Dermatitis calorica.

(c) Dermatitis venenata.

(d) Dermatitis medicamentosa.

**DEFINITION.**—Dermatitis or inflammation of the skin is a cutaneous disorder characterized by heat, redness, pain, and swelling; in other words, by the ordinary phenomena of inflammation.

#### **DERMATITIS TRAUMATICA.**

Under this head are included all forms of inflammation the result of mechanical violence to the skin, such as *contusions, lacerations, and excoriations* (due to *friction, pressure, scratching, etc.*). The traumatism produced by scratching is of especial importance to the dermatologist, as it commonly modifies cutaneous lesions, and, as the case may be, aids or obscures the diagnosis.

The inflammatory action is usually simple, unless the tissues become infected by staphylococci or streptococci, when pus formation or erysipelatous inflammation may follow. A common form of simple dermatitis is that resulting from chafing; while this, under the name *intertrigo*, is usually classed among the congestive erythemas, it more frequently runs into true inflammation.

The most frequent sites for the intertriginous dermatitis are the armpits, perineum, and insides of the thighs and the under-surfaces of pendulous breasts, especially in corpulent women. It is more frequent in summer than in winter, as free perspiration, macerating the upper layers of the skin, and undergoing decomposition, with the formation of irritant compounds, promotes the occurrence of the inflammation.

Intertriginous dermatitis is very frequent in infants and young chil-



dren, especially if great care is not taken to keep the genital and anal regions clean and dry. The most aggravated dermatitis of the genitals, insides of the thighs, and lower part of the belly may develop in a few hours in an infant allowed to lie in a wet and dirty napkin. The pain, itching, and burning are sometimes very intense, preventing sleep and keeping the child in a state of high, nervous tension, crying and irritable.

**Treatment.**—In simple traumatic dermatitis any soothing application will be useful. **Cold cream, oxide of zinc ointment,** or simple **vaselin** is usually sufficient to allay the inflammation. One of the best applications is **hot water**, applied for five or ten minutes several times a day. The water should not be merely warm, but as hot as can be borne without discomfort.

For *intertriginous dermatitis* the writer has found **black wash** the best application. Applied on lint saturated with the preparation, it usually gives prompt relief from the burning and pain and controls the hyperemia. A mild **calomel ointment**,  $\frac{1}{2}$  dram (2 Gm.) to the ounce (30 Gm.) of **vaselin**, is also useful. In other cases **Lassar's paste** is useful. This is made as follows:—

℞ *Acidi salicylici*. . . . . gr. x (0.6 Gm.).  
*Pulv. amyli*,  
*Zinci oxidi*. . . . . of each ʒij (8.0 Gm.).  
*Vaselin* . . . . . ʒss (15.0 Gm.).

M. et ft. pasta.

Great care should be taken that only the finest powdered salicylic acid be used in making this and other ointments containing it. The crystallized acid usually proves extremely irritating to an inflamed or sensitive skin.

For the moderate grades of intertrigo or chafing, a simple dusting powder of **starch** and **oxide of zinc** is generally sufficient, if the irritated skin be kept clean and dry. The interposition of a fold of lint or soft linen between opposing surfaces of skin is an aid to the cure as well as the prevention of intertriginous dermatitis (Rohé).

### DERMATITIS CALORICA.

This form of dermatitis is due to exposure to excessive heat (dermatitis ambustionis, burn), or to excessive cold (dermatitis congelationis, frost-bite, chilblain). Although the character of the irritant would appear to be different, we have in both forms, according to the severity of the inflammation, erythema, vesication, or gangrene, accompanied by severe pain. Burns and frost-bites, being in the nature of emergency accidents, are more commonly regarded as surgical conditions. (See SKIN, INJURIES OF.)

### DERMATITIS VENENATA.

Dermatitis venenata is commonly spoken of as a dermatitis due to contact with poisonous plants; in its broader sense it includes inflammation of the skin due to the chemical ingredients of any substance, vegetable, animal, or mineral. Among these may be mentioned acids or alkalies, croton oil, mustard, arnica, mercury, chrysarobin, formalin, cantharides, aniline dyes, etc. The dermatologist is more especially interested in the dermatitis produced by poisonous plants, chiefly the *Rhus toxicodendron*—poison ivy; the *Rhus venenata*—poison sumach or dogwood, and the *Rhus diversiloba*—poison oak.

The poisonous principle in rhus poisoning is believed to be a volatile substance known as toxicodendric acid.

A great variety of plants have been

found capable of producing a dermatitis in susceptible individuals.

The writer observed cases of plant poisoning due to the chrysanthemum, the poison sumach, fresh squill roots, arbor vitæ, and the Japanese lacquer derived from *Rhus vernicifera*. The subjects of these affections never connect them with their contact with the plant—the contact sometimes being of the briefest—and the differential diagnosis is, therefore, at times difficult. Hoffmann (Münch. med. Woch., No. 44, 1904).

The writer has observed a number of cases of a skin affection in men working in cement. Pruritus, swelling, and a papulous eruption, with a tendency to lichen and eczema, are the main features. The French call it "cement workers' itch." He advises rubbing lanolin or wax on the hands and forearms before going to work, and keeping the shirt buttoned at the neck. Some firms supply cotton gloves and protecting goggles to their workmen, especially those working in tunnels, etc. Martial (Presse méd., Aug. 8, 1908).

Case in which dermatitis followed the local application of cows' milk. The rash occurred with perfect regularity, coming out about fifteen minutes after the milk touched the skin, lasting at first an hour, then gradually existing a shorter and shorter time until after twenty-one days it ceased to appear. In appearance it was a bright-red blush, not raised, at times sharply circumscribed, at others with fading pink edges to normal skin. In extent it conformed quite closely to the area touched by the milk, either by running over the chin or cheek from the mouth or on the area to which milk was purposely applied. Steele (Yale Med. Jour., Nov., 1909).

The symptoms of intoxication from paraphenyldiamine (used to dye hair, furs, etc.) and other poisonous aniline dyes, may be divided into (1) toxic eruptions, dermatitis and urticaria; (2) gastrointestinal symptoms, such as nausea; (3) nervous

symptoms, sleeplessness, dizziness, weakness of the legs, epileptiform attacks, and syncope. In several instances death has resulted; also retrobulbar neuritis with impairment of central vision and a central scotoma for red and green have been observed. Aurantia or hexanitrophenylamin, used in the staining of cheap yellow shoes, may also cause an outbreak of dermatitis. F. C. Knowles (Med. Rec., July 29, 1916).

While a large number of drugs produce eruptions but relatively few affect all individuals; the same drug does not always produce the same form of eruption. The iodides and bromides usually cause an acneform eruption, and may cause more serious disturbance. The hypnotics produce eruptions of varying character. Arsphenamine sometimes causes a violent dermatitis with symptoms of nephritis. When a drug is being taken it should always be remembered in the presence of an unusual form of eruption. M. B. Hartzell (Trans. Pa. State Med. Soc.; N. Y. Med. Jour., Mar. 8, 1919).

**Symptoms.**—From a few hours to several days after exposure the hands, face, and genitalia (in a typical case) become the seat of innumerable, closely studded vesicles and blebs, accompanied by redness, swelling, and great burning or itching. The vesicles and blebs are at times angular or stellate, and not infrequently appear in linear streaks. The eruption may be carried to various parts of the body by autoinoculation. The dermatitis lasts ordinarily from one to four weeks.

Some individuals of both sexes are extremely susceptible to plant poisoning, so much so that proximity without contact suffices to bring on an attack. Other individuals enjoy comparative immunity. Some persons are susceptible at one period of life and become immune later, or the converse of this may be true.

Death from ivy poisoning in a man 42 years old after two months of intense suffering. Some persons are affected by merely passing the plant without coming in contact at all, while others can handle it with impunity. Case observed in a child 6 years old who died from the effects of severe ivy poisoning produced by having his skin rubbed while wet by the hands of a boy who had been rooting up plants of the poison ivy, and although the boy had previously washed his hands thoroughly, under supervision, first with soap and hot water, and afterward with vinegar. The boy who had been working with the plants had a full and apparently permanent immunity to poison ivy. Reynolds (Bull. of Chicago Health Dept., July 23, 1904).

When the face is involved, the eyelids are greatly swollen and the affection may simulate an erysipelas in appearance; the absence of high fever and other systemic symptoms will readily exclude the latter disease. In some cases considerable difficulty will be experienced in distinguishing rhus poisoning from an acute eczema. The history of previous similar attacks, exposure to plants, the presence of numerous closely aggregated pinpoint-sized vesicles, the high-grade edema present, and the more rapid involution will distinguish dermatitis from eczema.

Study of 187 cases of occupation dermatitis at the Royal Infirmary, Edinburgh: Most patients are attacked either a week or two after going to work for the first time or not until they have been employed a number of years. Seborrhea and hyperidrosis, or precedent skin disease, increase the liability to attack. Attacks are more frequent in hot weather, heat being a predisposing agent, and soaps also in many cases. Gardiner (Brit. Med. Jour., Oct. 24, 1908).

**Treatment.**—Immediately after exposure it is well to wash the skin with **soap and water** and follow such

ablution with the use of **alcohol**. It is alleged that much of the irritant principle can be thus removed and the inflammation aborted. The earlier that such treatment is employed, the better the result will be. At a later stage the following combination gives most satisfactory results:—

**R.** *Acidi borici*,

*Resorcin* .....āā ʒj (4 Gm.).

*Sodii hyposulphit.*..... ʒiij (12 Gm.).

*Glycerini* ..... fʒj (4 c.c.).

*Pulv. zinci oxid.*..... ʒiij (12 Gm.).

*Aquæ* ..... fʒviiij (240 c.c.).

**M.** Sig.: Apply every hour to the affected areas.

The writer recommends constant moist dressings of **ice cold boric acid solution**. The **larger blebs** are **opened**, but the smaller ones are not touched. Ointments should be avoided in the acute stage. J. E. Lane (Med. Rec., Sept. 11, 1915).

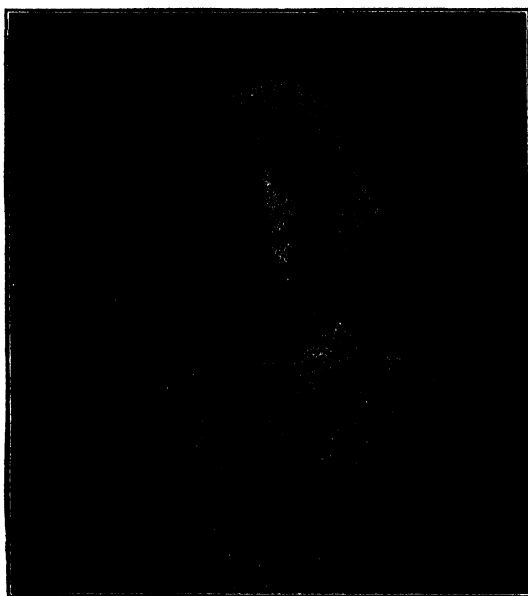
Wet compresses of a solution of **sodium hyposulphite**, 1 dram to the ounce, are also useful. Likewise, saturated solutions of **boric acid**, equal parts of **black wash** and **lime water**; **bromine** in **olive oil**, 10 minims to the ounce; **carbolated zinc ointment**, 5 to 10 grains to the ounce, and a host of other remedies.

The writer strongly advocates the following treatment: Mix 1 part of **ichthylol** with 1 to 3 parts of water and apply this on the affected area and for the space of an inch beyond by means of a tuft of absorbent cotton wound around a toothpick. The paint rapidly dries, forming a thin, elastic film. Glycerin must not be added, since it prevents drying. The affected parts should first be **washed with soap and water**, or, if an ointment has previously been applied, it should be wiped off with **benzin**. Small vesicles may be left undisturbed, but larger ones must be opened by cutting off the top with curved scissors. Successive layers of ichthylol form a skin, which peels off after a few days, leaving a more

or less healthy surface. If desired, the ichthyol may be washed off with soap and water at any time. H. G. Klotz (N. Y. Med. Jour., vol. lxxvi, No. 8, 1902).

In the treatment of ivy poisoning, the writer suggests the following method: No scratching; no ointments in the acute stage; no bandages, for these tend to spread the poison to adjacent surfaces; if any protector is necessary, it should be

The writer in his own case used **carron oil** poured frequently all over the body and more frequently patted over the worst places. This gave such relief that he continued its use till the end; whenever the itching became severe, he rubbed dry **bicarbonate of soda** into the skin, covered as it was with the carron oil. This seemed to be the best combination; the dry powder rubbed into the itching places would bring relief after the smarting



Case of dermatitis venenata, due to rhus poisoning. (Pisko.)  
American Journal of Dermatology.

a loosely applied dressing of absorbent cotton, kept moist at all times and changed at short intervals; frequent and copious washings with lukewarm water and an unirritating soap; in handling the inflamed surface it is best to wear rubber gloves; after the parts are washed, a 2 to 4 per cent. warm solution of **permanganate of potassium** should be applied. This completely neutralizes any poison with which it comes in contact; the strength of the solution and the frequency of application are matters of judgment with the physician; after the acute stage is past, ointments are permissible. A. W. Baird (Med. Rec., Aug. 7, 1909).

sensation had subsided. **Ice-cold compresses** were also very helpful.

A second kind physician gave him the following prescription, which he used with great benefit:—

℞ *Zinc oxide*,  
    *Magnes. carb.* of each 3j (8 Gm.).  
    *Thymolis iod.*..... 3j (4 Gm.).  
    *Aquæ caleis.*....q. s. ad 5iv (120 c.c.).

M. Sig.: External use.

After three weeks of suffering the rash disappeared, but scratching could easily bring back the typical rash. Ellis (Med. Rec., July 23, 1910).

The best remedy is still **lead and opium wash**, but improved. The improvement is a solution of **boric acid**

10 grains (0.6 Gm.) to the ounce (30 c.c.) of distilled water as a base, 5 grains (0.3 Gm.) acetate of lead, and in place of powdered opium the **liquor morphinæ sulphatis**, as suggested by Prof. William H. Thomson.

Internally the writer gives small doses of **aconite** and **gelsemium** for the fever and nervous disturbance, and **calomel**, **ippecac**, and **bicarbonate of sodium**, following the latter with a glass of water before breakfast. He sometimes adds to the same quantity of **Epsom salts** an equal amount of **cream of tartar**. Gardner (Med. Record, Aug. 20, 1910).

Recent studies have shown that the cause of the irritation may be counteracted with a **potassium permanganate** solution. Its application gives great relief and when used soon after exposure or as soon as the first vesicles appear will avert the distressing itching. Treatment should be as follows: First thoroughly wash the part or parts with warm water and soap; then apply an alkaline wash, such as a teaspoonful of **bicarbonate of soda** to 1 pint (500 c.c.) of water. Following this should come several washings in warm 2 to 4 per cent. solution of permanganate of potassium. The strength of the permanganate solution should vary according to the severity of the attack. (Med. Rev. of Rev., June, 1912.)

Berryhill, of the United States Navy, scrubs the inflamed skin freely with a brush and hot soapsuds and then applies alcohol. This method has been employed, with satisfactory results, by R. T. Morris, of New York (Jour. Amer. Med. Assoc., Sept. 30, 1911), except that ether was used instead of alcohol.

In the same number of the journal quoted John C. Hemmeter advises first an alkaline hot bath, this to be followed by liberal rubbing with an ethereal antiseptic soap solution. Then the affected parts are bathed with 85 per cent. alcohol and gently dried.

For the infective, secondary condition, Hemmeter applies the ointment of yellow oxide of mercury, to which

he adds basic morphine, 4 grains (0.26 Gm.) to the ounce (30 Gm.). These two applications are to be made in the morning. The distressing itching is relieved and the discharge dried up by an ointment composed as follows: **Bismuth subgallate**, drs. 5 (20 Gm.); solution of **epinephrin** (**adrenalin chloride**) 1:1000, m. 100; **lanolin**, dr. 1 (4 Gm.); **white petrolatum**, enough to make oz. 1 (30 Gm.). This is to be rubbed in liberally at nighttime and dusted over with an antiseptic powder. (Medical Standard, Aug., 1912.)

Hardaway, of St. Louis, recommends very highly a lotion of **zinc sulphate**,  $\frac{1}{2}$  dram (2 Gm.) to the pint of water. Fluidextract of **grindelia robusta**, either full strength or diluted with water in various proportions, is highly lauded by Van Harlingen and others. When the vesicles have ruptured, drying or absorbent powders of **starch**, **chalk**, **oxide of zinc**, **orris root**, **lycopodium**, etc., may be used with good effect. Astringent lotions, among which acetate of lead holds a high place, are especially useful when the eruption is fully developed.

The writer fed a cow with a mixture of grass and poison ivy plant. The milk of this cow was imbibed the next day. The test was made in August and there was immunity for the rest of the summer. About 1 pint of milk was taken for 2 days and no other treatment was instituted. The following summer the patient had 3 slight attacks. In these attacks **sal ammoniac** solution, 1 tablespoonful to a pint (500 c.c.) of water, was applied by means of compresses for several hours, and then hot **antiphlogistine** poultices. W. H. Dffenbach (So. Cal. Pract., June, 1917).

## DERMATITIS MEDICAMENTOSA.

This class includes eruptions due to the ingestion or absorption of medica-

ments. Drug eruptions are favored by (a) idiosyncrasy; (b) excessive cutaneous elimination; (c) imperfect renal and intestinal elimination (often due to renal or cardiac disease); (d) large doses; (e) long-continued administration. Individual susceptibility is the most important factor. The eruption may be macular, papular, vesicular, urticarial, bullous, or hemorrhagic.

*Acetanilide* in large or long-continued doses may produce cyanosis. It occasionally causes an erythematous or erythematopapular rash.

*Antipyrin*.—Out of 52 cases collected by Spitz, 41 were morbilliform, 4 urticarial, and 7 erythematopapular. Eruptions prone to itch and desquamate. I have seen a severe exfoliative dermatitis with loss of nails and hair following large doses of antipyrin.

*Arsenic*.—Urticarial eruptions most frequent; may, however, be erythematous, papular, or vesicular. Extensive pigmentation may follow long-continued use of arsenic; herpes zoster thought to be produced by it at times. Hyperkeratosis of the palms and soles may result from long-continued use and may eventuate in serious cutaneous cancer. Arsenical eruptions are relatively uncommon.

*Belladonna*.—Erythematous eruption resembling scarlatina. Not uncommon.

*Boric Acid and Sodium Borate*.—Rare. Erythematous, with small vesicles. Continued use may cause dry, scaly eruptions, with loss of hair.

*Bromine and Bromides*.—Pustular (acneiform) eruption is the most frequent type. In children, large, brownish-red, button-like nodules are not uncommonly seen and are quite characteristic. Bromide eruption may appear after the cessation of the adminis-

tration of the drug. An infant may absorb the drug through the maternal milk. Less common are macular, papular, urticarial, and bullous eruptions.

*Cantharides*.—Erythematous and papular eruptions, chiefly about genitals. Rare.

*Capsicum*.—Erythematous eruption. Rare.

*Chloral*.—A scarlatinoid erythema, with subsequent desquamation, may occur. More rarely urticarial, papular, or vesicular lesions.

*Copaiba and Cubeb*.—Not uncommon; most rashes following the combined use of these two drugs are due to the copaiba. Most common is a morbilliform rash strongly resembling measles. May also be scarlatinoid or urticarial, or, in rare cases, vesicular, bullous, or petechial.

*Digitalis*.—Rare. Scarlatiniform or maculopapular.

*Ergot*.—Rare. Vesicular, pustular, bullous, petechial, or gangrenous lesions.

*Iodine and Iodides*.—The pustular acneiform eruption, like that caused by bromides, is common. Bullous, erythematous, urticarial, hemorrhagic, papillomatous, and gangrenous lesions may rarely develop. As with the bromides, the eruption may appear after the drug has been discontinued.

*Iodoform*.—Absorption from wounds may cause grave symptoms and erythematous, papular, vesicular, bullous, or petechial eruptions.

*Mercury*.—Uncommon. Erythematous.

*Opium and its Alkaloids*.—Uncommon. Itching, erythematous rash, resembling measles or scarlet fever. At times urticarial.

*Potassium Chlorate*.—Rare. Macular and papular eruption.

**Quinine, Cinchona, etc.**—Most frequently erythematous, resembling scarlet fever. May be accompanied by some fever, and when eruption is well marked it is followed by pronounced desquamation. Throat is reddened, but not edematous. Of 60 quinine eruptions analyzed by Morrow, 38 were erythematous, 12 urticarial, 5 purpuric, and 2 vesicular and bullous.

**Salicylic Acid Group.**—Occasional. Erythematous and scarlatiniform, sometimes followed by desquamation. May be urticarial, purpuric, vesicular, or bullous.

**Strychnine.**—Scarlatiniform rash once observed.

**Sulphonal.**—Uncommon. Macular and erythematous. Rarely purpuric. The author observed a giant urticaria with great swelling of face follow a 20-grain (1.2 Gm.) dose in an alcoholic.

**Thallium Acetate.**—Experimental administration in animals has caused patchy baldness.

**Turpentine (Terebene).**—Uncommon. Erythematous, vesicular, and papular eruptions.

**Veronal.**—I have observed eruptions closely resembling the rashes of scarlet fever and measles. The scarlatinoid rash was accompanied by fever.

The tincture of arnica is so freely used as an external application to bruises and sprains that it may be useful to the practitioner to know that it sometimes produces a decided dermatitis, which may be accompanied by vesiculation. The cessation of the application and dressing affected part with a soothing or mildly astringent lotion (bicarbonate of soda, borax, sulphate of zinc) will generally suffice to restore the normal condition of the part.

Among other agents used for medicinal purposes which produce dermatitis of varying intensity are mustard, cowhage, chrysarobin, ipecac,

capsicum, mezereum, thapsia, cantharides, oil of turpentine, tar, creosote, paraffin, petroleum, pyrogallol and salicylic acids, chloral hydrate, sulphur, iodine, mercurial preparations, and the more active alkaline, acid, and mineral caustics.

The knowledge may also be useful that the juice of the common buttercup of the fields and the garden nasturtium may cause inflammation of the skin. Rohé (Sajous's Cyclopedia, vol. ii, p. 409, 1903).

JAY F. SCHAMBERG,  
Philadelphia.

## DERMATITIS, Infrequent Forms of.

—Besides the forms described under the preceding heading there are others which are less frequently met with, though of sufficient importance clinically to merit a description in these columns. The forms described are those selected by the former associate editor of this department, the late Dr. Geo. H. Rohé, whose versions have been brought to date.

### DERMATITIS HERPETIFORMIS, or Duhring's Disease.

**Definition.**—As defined by Duhring this form is characterized by an inflammatory, superficially seated, multiform, herpetiform eruption, or erythematous, vesicular, pustular, and bullous lesions, occurring usually in varied combinations, accompanied by burning and itching, pursuing usually a chronic course with a tendency to relapse and recur.

**Symptoms.**—There are five varieties of the disease, namely, the erythematous, vesicular, bullous, pustular, and multiform, indicating the prevailing type of lesion present.

There is usually a prodromic febrile stage, which, however, rarely amounts to more than slight chilliness, flushing, or heat, with the accompaniments of malaise and constipation. Itching may precede the outbreak of the eruption. Any one variety of lesion may appear, or there may be from the beginning a combination of two or more of them. The type of lesion may change during the course of the disease, or, as is more rare, may remain constant throughout the attack, and may also show the same fea-

ures in subsequent attacks. The subjective sensations are burning, itching, and prickling, which may be severe. In one case of the vesiculopustular variety, the itching and burning were most intense, relief being obtained only after the application of strong ointments or lotions of cocaine.

Fourteen cases in which indican was found in marked excess in the urine. Six of these were studied by

remedies had failed. Engman and Davis (Jour. Amer. Med. Assoc., Feb. 12, 1916).

The *erythematous* variety occurs in patches or diffused over the surface. There is usually slight elevation of the affected skin. The red color of the eruption may be varied by a yellowish or brownish tint, and is usually followed by more or less pigmentation.

The *vesicular* variety is the most com-



Case of bullous dermatitis herpetiformis. (Gardner.)  
British Journal of Dermatology.

the writer. M. F. Engman (Jour. of Cutan. Dis., May, 1906).

Dermatitis herpetiformis indicates in certain skins a general toxemia, such as indicanuria or intestinal putrefaction. Tobacco and its excessive use is the cause of toxemia in other cases. Each case of dermatitis herpetiformis, therefore, is a study in itself to search out the source of the toxemia. The writers have been studying the mouth in this disease including pyorrhea. In the latter they tried *emetine* in  $\frac{1}{2}$ -grain (0.03 Gm.) doses daily for 5 or 6 doses, in 4 cases with success, where other

mon. The vesicles are irregular in size and shape, usually tense, and rising abruptly from an apparently normal base. They may be disseminated or aggregated in groups or clusters. They sometimes coalesce to form small blebs. The itching is usually more intense than in other forms of eruption. After the vesicles rupture relief is often obtained.

In the *bullous* variety the bullæ are usually tense, standing out from the level of the skin. They are usually irregular in outline, differing from the bullæ of pemphigus. They are also more likely to appear in groups or clusters. Vesicles and pustules may accompany the blebs.



The *pustular* form appears pustular from the beginning. The lesions are either acuminate, discrete, up to a pea in size, or flat, not elevated above the skin, aggregated in small groups, and miliary in size. The larger pustules often have a puckered appearance.

The *multiform* variety is made up of all the various types of eruption in combination, and has suggested one of the names by which the disease is known, viz., *dermatitis multiforme*. The lesions are macules, papules, vesicles, pustules, and bullæ of all shapes and sizes. There are excoriations and pigmentations of a brownish color. The character of the lesions is constantly changing.

The course of the disease is a chronic one, and it may last, appearing and disappearing at intervals, for many years.

Vaccination may, in certain cases, be the exciting cause of the eruption; not in the sense of an infection, but as one of probably many agents which may produce this train of symptoms in certain people. Certain regions of the body are especially affected by the eruption, viz., the parts about the nose, mouth, and eyes, the backs of the hands and wrists, the backs of the ankles and feet, and the genital region. Unna's hydroa puerorum is to be placed by itself, either as a distinct variety of dermatitis herpetiformis or as an independent affection. J. T. Brown (Jour. of Cutan. Dis., Sept., 1905).

Case of recurrent dermatitis herpetiformis in which the patient had had 8 successive attacks of the disease in 4 years, with intervals of several weeks between the outbreaks. He now shows over the entire body typical, grouped lesions consisting of vesicles, ruptured and unruptured, on erythematous bases; there is also a great deal of crusting and excoriation. This patient had had 2 strongly positive Wassermann tests at intervals of 4 months, but denies syphilis both by history and symptoms. Buford (Boston Med. and Surg. Jour., June 8, 1916).

**Etiology.**—It sometimes begins in childhood, but most frequently between 30 and

40 years of age. There seems to be some connection between the disease and instability of the nervous system, but nothing is definitely known upon this point. There seems to be a frequent relation between the eruption and pregnancy, the puerperal state, or menstrual disturbances. The disease described by Bulkley and others as "herpes gestationis" is probably a vesicular or vesiculobullous form of D. herpetiformis occurring during pregnancy. There seems, also, some connection between renal defect and D. herpetiformis. It has been observed after septic infection.

**Pathology.**—The pathological histology of dermatitis herpetiformis has been most thoroughly studied by Gilchrist, and the histological characters of the affection are shown in the annexed illustrations representing sections from a case of dermatitis herpetiformis (Duhring).

**Diagnosis.**—The multiformity of the lesions and the tendency to their herpetetic arrangement, which Duhring regards as characteristic; the chronicity of the disease, and its frequent recurrence; the burning and itching, and general absence of marked constitutional disturbance will usually enable a diagnosis to be made without difficulty. Among the diseases which may cause doubt are pemphigus, herpes, erythema multiforme, and eczema.

**Prognosis.**—The prognosis, so far as life is concerned, is usually favorable, but the disease is generally chronic in duration, and has a marked tendency to recur. Duhring has reported cases lasting thirteen and fourteen years.

**Treatment.**—The treatment of dermatitis herpetiformis is far from satisfactory. In some cases the lesions yield promptly to local applications, while in others, as Duhring states, the lesions develop, relapse, and recur from time to time in spite of the most varied measures employed. The internal treatment should be directed toward the improvement of the general health, and the ascertainment and removal, if possible, of disease or disorder of the stomach, intestines, or kidneys. The apparent close connection of the nervous system with the etiology of the disease would lead one to expect benefit from neurotic remedies, such as arsenic, phosphorus, and strychnine. Unfortunately,

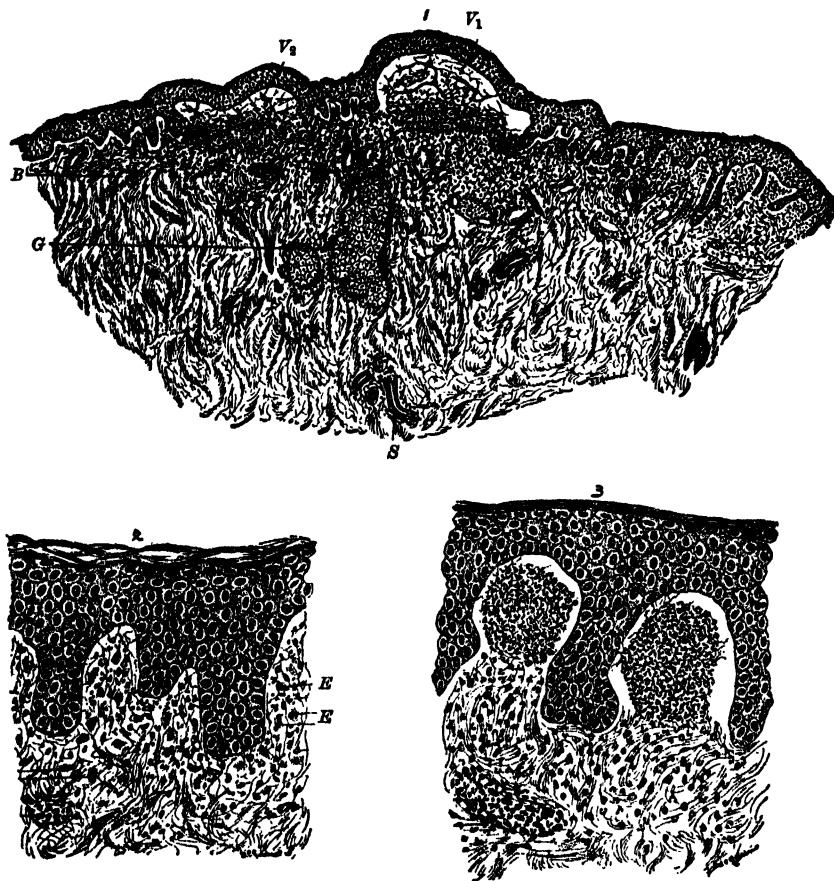
neither of these can be relied upon in all cases, though some show distinct improvement after the use of the first-named.

**Cannabis Indica**, chloral, opium, and antipyrin have been tried as sedatives and anodynes; but little benefit can be expected from them.

Local applications likewise are often

but have apparently little influence upon the progress or duration of the eruption. A 2 per cent. ointment of cocaine is also of value as a local anodyne when the burning and itching are severe.

Ichthyol, resorcin, carbolic acid, salicylic acid, and thiol have been used, but without much success. A hot bath before re-



Sections from a case of dermatitis herpetiformis. (Gilchrist.)

disappointing. Duhring has had most success—in the vesicular, bullous, and pustular forms—from a strong **sulphur ointment**, 2 drams (8 Gm.) to the ounce (30 Gm.), applied with sufficient friction to rupture the lesions. In the erythematous form soothing applications are indicated. **Tar**, in the form of **liquor picis alkalinus**, 1 dram (4 Gm.) to 8 ounces (240 c.c.) of water, or liquor carbonis detergens of the same strength may be used with benefit in some cases. They relieve the itching,

tiring sometimes gives grateful relief from the subjective symptoms.

Case in a male child commencing at the age of 9 months and continuing to the time of the report, when the patient was  $3\frac{1}{2}$  years of age. An improvement occurred when the child was about 12 months old, followed by recrudescence, a milder attack lasting about five weeks. The eruption has since occurred three or four times every year, lasting for two

to six weeks. The trunk and limbs have been attacked; the face, scalp, and mucous membranes have always escaped.

The writer in this and certain other cases of dermatitis herpetiformis administered **thyroid gland** in small doses. He rarely gives more than 1 grain (0.06 Gm.) of an active, reliable preparation three times daily, and continues it during considerable periods of time. In the case under observation  $\frac{1}{16}$ -grain (0.01 Gm.) doses of the thyroid preparation have been administered. R. L. Sutton (Amer. Jour. Med. Sci., Nov., 1910).

The writer withdrew 20 c.c. of the **patient's own blood** and injected it into the muscles of the buttock in 30 cases of skin-disease, including dermatitis herpetiformis. The pruritus was often influenced on the following day. The same dose was usually repeated in 4 days, and a third injection given, if necessary, on the 7th day. P. Ravaut (Ann. de Derm. et de Syph., May, 1913).

### DERMATITIS GANGRENOZA.

**Definition.**—Inflammation of the skin accompanied by sloughing or gangrene.

**Etiology.**—Gangrene or sloughing may follow any lesion of the skin severe enough to destroy its vitality. Thus it sometimes follows intense or long-continued pressure, severe contusions, violent inflammation, or some profound nervous disturbance. The ordinary bed-sore is an example of gangrenous dermatitis from pressure; the acute or neurotic bed-sore follows a neuritis or other disease of the peripheral nerves. In severe contusions, the application of caustics, deep burns, or frost-bite the slough is due to the sudden and violent arrest of nutrition in the part. Diabetes is not rarely accompanied by gangrene. The interesting affection known as Raynaud's disease, whose most marked manifestation is symmetrical gangrene of the extremities, cannot properly be described as a gangrenous dermatitis.

A gangrenous dermatitis of infants has been described under various names. It occurs most frequently after varicella in children debilitated by innutrition or constitutional dyscrasia. The lesions consist

of ulcerations under a black slough of varying thickness, and occupying the site of one of the pustular or bullous lesions of the disease. The same lesion is not infrequently observed in vaccination, especially with bovine lymph. It is probable that the gangrene is due to an infection by micro-organisms, but the nature of these has not been determined. This form of localized gangrene may also follow other skin diseases.

**Treatment.**—The treatment of gangrenous dermatitis consists in the application of **stimulant and antiseptic lotions or ointments**. Kessler found **pyoktanin** applied locally very efficient in this form of dermatitis. **Ichthyol** and a solution of **iodine** may also prove useful.

### DERMATITIS MALIGNA.

**Definition.**—An inflammation of the skin with a tendency to malignant degeneration often restricted to the nipple.

**Symptoms.**—The terms "malignant dermatitis" and "malignant papillary dermatitis" are applied to an inflammation almost exclusively limited to the mammary portion and areola of the mammary gland, and generally known as "Paget's disease of the nipple." It has much the appearance of an eczema rubrum, and is nearly always followed by epitheliomatous infiltration.

Of the 18 cases reviewed by the writer, no less than 9 occurred on the external genitalia, and 5 affected the glans penis. It will thus be noted that this disease is by no means to be regarded as confined exclusively or largely to the female breast and nipple and areola in particular, as first described by Paget, and subsequently designated by other writers as "Paget's disease of the nipple." M. B. Hartzell (Jour. of Cutan. Dis., Aug., 1910).

Sir James Paget, who first described the affection in a classical paper in the St. Bartholomew's Hospital Reports for 1874, gives the following account of its clinical history:—

"The patients were all women, varying in age from 40 to 60 or more years, having in common nothing but their disease. In all of them the disease began as an eruption on the nipple and areola. In the majority it had the appearance of a florid,

intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed; like the surface of very acute diffuse eczema, or like that of an acute balanitis. From such a surface, on the whole or greater part of the nipple or areola, there was always copious, clear, yellowish, viscid exudation. The sensations were commonly tickling, itching, and burning, but the malady was never attended by disturbance of the general health. I have not seen this form of eruption extend beyond the areola, and only once have seen it pass into a deeper ulceration of the skin after the manner of a rodent ulcer. . . . But it has happened that, in every case which I have been able to watch, cancer of the mammary gland has followed within, at most, two years, and usually within one year. The eruption has resisted all treatment, both local and general, that has been used, and has continued even after the affected part of the skin has been involved in the cancerous disease."

The only fact that can be added to this description, after twenty-four years' further observation, is that the disease is not exclusively located upon the nipple of women, but that it may involve the nipple of the male or may occur upon other portions of the body. The inflamed patch of the nipple and areola is usually decidedly indurated, with an elevated border, and gives the sensation, when pinched up, of a button inserted in the skin.

Paget's disease of the nipple was described by Velpeau many years before Paget's article appeared. The disease has a number of other names but no other has been universally adopted. To Paget belongs the credit for a clear, concise description of the condition, which has always received a great amount of attention from surgeons, pathologists, and dermatologists, in spite of the fact that it is a rare disease. About 150 cases have been published up to this time; 18 extra mammary cases were collected in 1910; the others were located on the breast.

The writers had the opportunity of studying 5 cases of true Paget's disease, and a number of others simu-

lating it which were excluded as the result of their histological findings. The conditions which simulate Paget's disease and are often mistaken for it include eczema, primary cancer with excoriation or ulceration of the nipple or of the skin, papillary cystadenoma, the rare form of diffuse cancer before mentioned, and one or more types of the rare primary tumors of the nipple. Ulcerated scirrhus furnishes the greatest number of mistaken diagnoses. The microscopic examination confirms or refutes the diagnosis in all cases. Jopson and Speese (*Annals of Surg.*, lxii, 212, 1915).

The writers found reports of over 200 cases in the literature. Of these, 30 have been recorded as extramammary Paget's disease, including lesions of the back, nose, lip, and genitalia.

The earliest symptom appears usually as a pimple, a crack, a red patch, a scab, or an excoriation. Paget distinguished two general types: one, weeping eczematous, the other, dry psoriatic. These may be mixed. Often a burning and tingling sensation is complained of, but rarely pain. The borders are always well defined, and according to some authors this is the only diagnostic sign by which it can be differentiated from ordinary eczema. S. Sekiguchi (*Annals of Surg.*, lxxv, 175, 1917).

**Pathology.**—It is not definitely known whether the disease is epitheliomatous from the start, or whether it begins as an eczematous dermatitis and becomes malignant in consequence of the epitheliomatous degeneration of the skin. The glandular structures of the nipple are especially liable to malignant degeneration, and it is probable that any long-continued irritation of the epithelial elements would be followed, in persons with a predisposition to epithelial overgrowth, by malignant disease. Upon this assumption, the view that the primary disease is an eczema or a dermatitis, and that malignancy is secondary, is a rational one.

Microscopic studies of the disease by Thin and Wile have shown the epithelial

infiltration present at a very early stage. It may be said, however, that when the diagnosis of malignant dermatitis or Paget's disease can be made the trouble is no longer an eczema, whatever it may have been at an earlier period.

**Diagnosis.**—Diagnostic features of malignant dermatitis as differentiated from eczema of the nipple are:—

1. Its occurrence in women over 40 years of age, while eczema of the nipple is more frequent in the child-bearing age, and especially during lactation.

2. The affected surface is red, raw, and granular-looking.

3. There is decided superficial, well-defined induration in place of the diffuse, leathery infiltration of eczema.

Finally, while eczema is often obstinate, it usually yields to proper local treatment; while malignant dermatitis is not curable by any means short of cauterization or removal with the knife.

**Treatment.**—In reference to the treatment of malignant dermatitis, Sir James Paget said in his paper above referred to: "In practice the question must be sometimes raised whether a part, through whose disease or degeneracy cancer is very likely to be induced, should not be removed. In the member of a family in which cancer has frequently occurred, and who is at or beyond middle age, the risk is certainly very great that such an eruption on the areola, as I have described, will be followed within a year or two by cancer of the breast. Should not, then, the whole diseased portion of the skin be destroyed or removed as soon as it appears incurable by milder means?"

According to recent investigations, Paget's disease of the nipple is cancerous from the very first, rapidly involving the skin and the breast itself. The practical result of this conclusion demands for Paget's disease the same prompt attention and radical surgical interference as is accorded all other cancers of the breast. There is a striking parallelism between Paget's disease of the nipple and leucoplakia in cancer of the tongue; and also an analogy with certain cancers of the scrotum and penis, occurring in certain working

classes. Jonas (*Interstate Med. Jour.*, Sept., 1910).

The answer to the question is self-evident, in view of the history of the disease. If a diagnosis of malignant dermatitis is positively made, there can be no other rational treatment than such as would be appropriate for epithelioma; namely, destruction of the diseased skin by **cautery** or **caustics**, or **removal** of the entire **breast**. In cases of doubt, the approved remedies for eczema may be tried, but too much time should not be wasted in temporizing expedients. The **X-rays** may be tried, several cases of cure by this agent having been reported. That the benefit was but temporary in most of these, however, is probable. After **removal** of the **growth**, however, **X-rays** may prove useful to prevent recurrence.

Study showed that the logical treatment of the nipple affection should be that of cancer of the breast. In operable cases where the diagnosis is beyond doubt, **amputation** of the **breast**, followed, if deemed advisable, by **X-rays**, offers, in our opinion, the best chance of recovery. F. E. Simpson (*Quarterly Bull. N. W. Univ. Med. School*, June, 1909).

**Pyrogallie acid ointment**, 3 drams (12 Gm.) to the ounce (30 Gm.); **lactic acid**; **chloride of zinc paste**, of varying strength; **chromic-acid** and **arsenical pastes**, the best of which is **Marsden's** (*R. acidi arsenosi, pulv. g. acacia*, of each, p. e.; mix and make a stiff paste with water just before using), may all be used with good effect. **Chromic acid** in concentrated solution is the least—Marsden's paste the most—painful of these applications. The arsenical paste should not be applied over a surface of more than one square inch at a time, as otherwise sufficient arsenic may be absorbed to cause symptoms of poisoning. The pain of the application is very severe, and, as the caustic must remain upon the part at least twenty-four hours, the suffering is always considerable. When the paste is applied a piece of lint is pressed upon it, which absorbs the surplus and prevents its spreading. After twenty-four hours, a poultice is applied, which soon causes a separation of the slough. The resulting

ulcer is usually healthy in appearance and heals readily under simple applications, if all the degenerated tissue has been destroyed.

The **galvanocautery** and **thermocautery** are trustworthy methods for destroying the morbid tissue.

When the area involved is large, the best treatment is thorough **extirpation** of the entire breast.

### DERMATITIS EXFOLIATIVA.

**Definition.**—Inflammation of the skin, acute or chronic, accompanied by exfoliation of the epidermis.

**Varieties.**—(A) Acute exfoliative dermatitis of infants. (B) Chronic general exfoliative dermatitis. (C) Local exfoliative dermatitis. (D) Epidemic exfoliative dermatitis.

#### (A) Acute Exfoliative Dermatitis of Infants.

**Definition.**—An acute inflammatory affection of the skin of infants, accompanied by exfoliation of the epidermis in flakes, running a rapid course, and in most cases ending fatally.

**Symptoms.**—The disease was first described by Ritter von Rittershain, who had observed nearly 300 cases in the course of ten years.

The children attacked were nearly all between 2 and 5 weeks old. A prodromal stage, characterized by abnormal dryness of the integument, with furfuraceous epidermal desquamation, usually occurred. The skin of the lower part of the face, especially about the angles of the mouth, becomes red and slightly tumid. The margin of the redness, which rapidly spreads, is indistinct, not being sharply defined against the healthy skin. The skin at the angles of the mouth becomes fissured and covered with scabs. The mucous membrane lining the pharynx and buccal cavity is reddened, and the palatal arch is the seat of superficial erosions, covered by a grayish-white exudation.

A study of the literature and a personal case showed an unmistakable connection between exfoliating dermatitis and pemphigus in infants, and the writer reports an additional convincing experience. It suggests that the germ causing the exfoliating dermatitis in the infants induced

pemphigus in the older children. Wirz (Correspondenzbl. f. schweizer Aerzte, Dec. 9, 1916).

The appetite and digestion remain unimpaired. There is no fever. The redness and thickening of the skin extend over the entire body. The face becomes covered by yellowish, translucent scabs upon a reddened base, intersected in various directions by fissures. The skin becomes wrinkled, and the upper layer separates from the cutis. The epidermis may be detached in large flakes or in scales. This process, continuing until the entire surface is denuded of epidermis, presents an appearance similar to that following an extensive scalding. In favorable cases the dark, raw-flesh color of the cutis soon gives way to a lighter red, and in some cases the normal color of the skin is restored in twenty-four to thirty-six hours. In unfavorable cases, on the other hand, the color is a dirty brownish red, and the cutis becomes dry and parchment-like. In those cases which terminate in recovery, the normal condition is entirely re-established in a week or ten days, the skin for a few days being covered by a fine, branny desquamation.

As sequels, eczemas of considerable extent, or small, superficial boils and abscesses, sometimes in large numbers, occur, and delay recovery. At other times extensive phlegmonous infiltrations occupy considerable tracts of skin, and may result in gangrenous destruction of tissue and death. In the latter conditions pneumonia and colliquative diarrhea not rarely precede the fatal termination. Relapses are rare. The disease is ascribed to a septic or pus infection localized upon the skin.

The writer observed 15 cases of exfoliative dermatitis in the newborn and examined the bladder contents bacteriologically in several. In all of them he found staphylococci both microscopically and by culture. In one case he found *Staphylococcus pyogenes albus* in the blood. The affection seems to belong, therefore, in the group of staphylococcic pyodermias thus explaining its ready transmission and emphasizing the importance of isolation of such cases.

Sperk (Zeit. f. Kinderheilk., xi, No. 1, 1914).

**Diagnosis.**—In typical cases, no difficulty should occur in diagnosis. Erysipelas, which sometimes closely resembles this disease, is easily excluded by the high temperature of the former. In pemphigus there are distinct bullæ separated by normal skin. In exfoliative dermatitis the redness and thickening spread and finally occupy the entire surface.

In a paper on the transmissibility of exfoliating dermatitis in the newly born, the writer observed within 2 weeks, 3 cases fatal by the ninth to the seventeenth day. The clinical picture was the same in all, and each had been breast fed. Rittershain had 297 cases at Prague in 10 years' experience. He and others regard it as an affection limited to early infancy and non-contagious. Others regard pemphigus of the newly born and exfoliating dermatitis of the newly born as the same process, differing merely in its intensity. The writer has been unable to find in the literature any history of direct transmission from skin to skin but has met with a case of this kind in his practice. Wolf (Jahrbuch f. Kinderheilk., Oct., 1915).

**Prognosis.**—This is decidedly unfavorable. In Rittershain's cases the mortality was about 50 per cent.

**Treatment.**—No internal treatment is indicated in uncomplicated cases. **Sufficient nourishment** is, of course, important. Locally, **cool baths**, or **bran baths**, afterward drying the skin with fine, soft cloths and carefully avoiding friction, will meet the indications in most cases. Ragged and loose patches of epidermis should be clipped off with scissors, and all denuded and fissured surfaces dusted with finely powdered calomel. The crusts which accumulate at the angle of the mouth and render nursing difficult and painful are best got rid of by soaking with **oil of sweet almonds** and carefully removing the loose ones by means of dressing forceps. **Slightly astringent baths** (decoction of **oak-bark**, 1 pint to the bath) are sometimes beneficial.

The writers observed the case of a man of 25 years, who had had psoriasis from childhood until 2 years before, where, after a severe course of chrysarobin treatment, the condition changed to one of exfoliative dermatitis. The entire body surface was red and covered with large, regular scales which were produced in great profusion. Four doses of **salvarsan** were given intravenously, but this did not do as much good as **thyroid extract**, which was begun in doses of 2 grains (0.12 Gm.) and gradually increased up to 15 grains (1 Gm.), 3 times daily. This was taken for a fortnight without any pulse acceleration or mental disturbance, the patient being kept in bed. The dose was later reduced to 5 grains (0.3 Gm.). Locally, a **zinc oxide ointment** with 2 to 3 per cent. of **salicylic acid** was used. Marked improvement occurred, all tendency to scaling disappearing. Molesworth and Verge (Austral. Med. Gaz., Aug. 31, 1912).

#### (B) Chronic General Exfoliative Dermatitis.

**Definition.**—A chronic generalized dermatitis, accompanied by constant exfoliation of the epidermis in dry, papery scales: the pityriasis rubra of Hebra.

**Symptoms.**—The disease begins with the appearance of red patches, gradually increasing in size, uniting with others until finally the entire surface is a sheet of red, dry skin. There is no thickness or infiltration. In about a week the epidermis begins to scale off in large, thin, white or grayish scales, which soon become very profuse and shed in large sheets. The skin at the same time becomes of a dusky or brownish red. The inguinal glands also enlarge. Later the skin becomes infiltrated to some extent, and looks tense and shiny in places. The mouth becomes puckered, and the skin of the joints may be fissured and sometimes moist. There may also be boils or pustules, the hair may fall out, and the nails atrophy and exfoliate. There is often fever at the beginning and at intervals during the course of the disease. There is little itching. The subjective

symptom mostly complained of is a sensation as if the skin were too small, and the patient frequently is chilly.

The course of the disease is chronic, lasting months or years, with exacerbations of greater severity, alternating with remissions.

There is usually progressive emaciation, and the patient dies of inanition, or is carried off by some intercurrent affection. Happily the disease is rare.

The cause of chronic general exfoliative dermatitis is not known.

**Diagnosis.**—The only disease likely to be mistaken for chronic exfoliative dermatitis is scaly eczema. Still, this is never so universally distributed; has usually a history of moisture and exudation at some time in its course; is attended by intense itching and considerable infiltration. Lichen planus is a papular disease, and, while the papules are sometimes aggregated in solid sheets, has a different history from this disease.

**Treatment.**—The treatment is unsatisfactory. Arsenic, which seems indicated, has little effect on the course of the eruption. Good results are sometimes obtained from codliver oil, both internally and externally. Saline diuretics and aperients are occasionally beneficial. Externally bland ointments may be applied. The extensive surface involved prohibits the use of mercurial applications, as salivation would be likely to follow. Glycerite of starch or Lassar's paste may at times relieve the uncomfortable sensation of tightness of the skin.

#### (C) Local Exfoliative Dermatitis.

**Definition.**—A localized dermatitis of mild character, occurring in rounded or oval spots; rosy, red, or mottled in color, and attended by furfuraceous desquamation. It is the pityriasis rosea of Gilbert and Duhring.

**Symptoms.**—The most thorough study of the disease in this country is by Duhring. It begins with the eruption of small macular or maculopapular lesions, of a rosy or reddish color, sharply defined against the surrounding skin, being sometimes on a level with it, sometimes slightly raised, and sometimes depressed. The patches are covered with fine, branny scales and spread at the margin while

healing in the center. The subjective symptoms are usually slight, only moderate itching being sometimes complained of. The disease lasts from one to three months, recovery taking place spontaneously.

**Causation.**—It is apparently a vegetable parasitic affection, but no characteristic parasite has been demonstrated in the skin or the scales.

**Diagnosis.**—The erythematous syphilide most nearly resembles this affection. The history of the case or observation of the patient for a week or two will clear up the diagnosis.

**Treatment.**—Lassar's paste or other mild salicylic acid or carbolic acid ointment may be used. Sulphur is also recommended. As the disease gets well of itself in a short time, not much attention need be given to the treatment.

#### (D) Epidemic Exfoliative Dermatitis.

This has recently been described by Thomas Savill, of London, who observed a large number of cases in the Paddington Infirmary. The disease begins as an erythematous or papular eruption, spreading peripherally like ringworm. This is followed by exudation and desquamation. The skin is red, thickened, and indurated, the epidermis being shed in flakes or scales. There is moist exudation in most cases, especially in the flexures of the joints or behind the ears. Exfoliation is continuous.

As the disease subsides, the skin becomes brownish, indurated, and thickened, and may be smooth and shiny or cracked. The hair and nails fall. There is itching and burning, sometimes severe. Albuminuria is frequent (50 per cent. of cases). There may be fever, although this is usually not high. It is most frequent in adults, generally in those of advanced age. According to Savill, dermatitis exfoliativa is the only skin malady which, up to the present time, has been connected with epidemic causes. In some respects it resembles eczema. The distinctive points are shown on the following page.

**Prognosis.**—This is grave. In Savill's experience over 12 per cent. died.

**Etiology.**—This is not known, though from its epidemic prevalence, apparent



## ECZEMA.

1. Attacks all ages, and children are very liable.
2. Gout is a marked predisposing cause.
3. Constitutional disturbance always moderate, and never fatal.
4. Dried crusts thrown off, but exfoliation of cuticle not a marked feature of the disease. Dermal thickening absent or moderate.
5. Course not definite.
6. Not hitherto regarded as contagious or epidemic.

## EPIDEMIC EXFOLIATIVE DERMATITIS.

1. Children almost exempt; old people especially prone.
2. Gout offers no predisposition.
3. Constitutional disturbance often severe, and may be fatal.
4. Epidermal exfoliation a constant feature. It may occur in some places without previous eruption. Dermal thickening generally present.
5. Course fairly definite.
6. Undoubtedly contagious and epidemic under certain conditions.

contagiousness, and great fatality it seems to be due to some infectious organism. This has, however, not yet been demonstrated.

**Treatment.**—Savill obtained most benefit from **creolin baths** (2½ pints of a 1 per cent. solution in a bath of 15 gallons of water at 95° F.—34.9° C.) or **creolin ointment** (½, 1, and 2 per cent.). The baths should be given once or twice a day.

The writer has found most useful prolonged (in those cases where conditions permit) permanent **warm baths**.\* After coming out of the bath the patient should be **enveloped in flannel soaked with either codliver oil or olive oil**. Foster (Jour. of Cutan. Dis., April, 1907).

In December, 1915, M. Brocq suggested to Desaux (Annales de Dermat. et de Syph., Mar., 1918) the study of "a somewhat special dermatosis of aspect, contour, and evolution, simulating seborrheic eczema," the extraordinary frequency of which around wounds of war and fistulæ had been noticed by him. In its fully-developed stage the dermatitis forms a plaque, with sharp polycyclical margins, bordered by a collarette and encircled by an inflammatory zone. The plaque is of a vivid red color, with abundant serous oozing, which, secondarily, becomes purulent and partly dries to form superficial crusts and a deeper grey adherent membrane. It extends peripherally "like an oily stain," disappears with antiseptic applications, is sometimes accompanied by glandular swellings, but never causes any general febrile reaction.

Perrin, Brocq, and Sabourand, who have studied these dermatoses, have regarded them as streptococcal impetigoes with secondary infection due to the golden staphylococcus, and the histological and

bacteriological study made by Desaux has confirmed these conclusions. For the most part it is the streptococcus of the wound or fistula which produces the dermatitis by infecting the cicatrix traumatised by antiseptics, or the neighboring skin which has been reduced to a state of lowered resistance by maceration, by fomentations, or possibly by X-ray examinations. The staphylococcus appears later and modifies the eruption, making it purulent. Eventually the streptococcus disappears and there is found only a diplococcus with porcelain culture, which is probably a modification of the golden staphylococcus, together with, in old eruptions, large forms of the polymorphic coccus of grey culture.

**Treatment** of the established dermatitis, according to Desaux (Presse méd., Mar. 30, 1916) after removing scales with **moist dressings**, consists in tearing off any remaining epidermis and applying to the entire affected area, with special care at its periphery, a 1 per cent. solution of **silver nitrate** followed by **Credé's ointment** or a 10 per cent. ointment of **collargol**. The silver solution should then be increased to 2, and even 5, per cent. After a few days, the affected area has been disinfected, but is still infiltrated, red, shining, and weeping. At this stage the following is used:—

℞ *Picis carbonis loti*. .... gr. xv (1 Gm.).  
*Ichthyolis* ..... 3ss (2 Gm.).  
*Zinci oxidi*,  
*Adipis lanæ hydrosi*. . . . . 3iiss (6 Gm.).  
*Petrolati* ..... 3ij (8 Gm.).

M. Fiat unguentum.

Five or six days later the area should be completely dried by painting with washed **coal tar**, to be left on 48 hours. The **tar-ichthyol** ointment should then be reapplied. To prevent extension, the healthy surrounding skin should be kept covered with the following:—

℞ *Camphoræ pul-*  
*veris* ..... gr. xiiss (0.75 Gm.).  
*Acidi borici*,  
*Ichthyolis* ..... 3iiss gr. xv (1 Gm.).  
*Zinci oxidi*,  
*Adipis lanæ hy-*  
*drosi* ..... 3iiss (6 Gm.).  
*Petrolati* ..... 3ij (8 Gm.).

M. Fiat unguentum.

S.













